IN THE CIRCUIT COURT OF THE FIFTEENTH JUDICIAL CIRCUIT IN AND FOR THE COUNTY OF PALM BEACH STATE OF FLORIDA

THE STATE OF FLORIDA, LAWTON M. CHILES, JR., Individually and as GOVERNOR OF THE STATE OF FLORIDA, DEPARTMENT OF BUSINESS AND PROFESSIONAL REGULATION, THE AGENCY FOR THE HEALTH CARE ADMINISTRATION, and DEPARTMENT OF LEGAL AFFAIRS,

COPY

Plaintiffs,

vs. CIVIL ACTION NO. 94-1466 AH

THE AMERICAN TOBACCO COMPANY; R. J. REYNOLDS TOBACCO COMPANY; RJR NABISCO, INC.; B.A.T. INDUSTRIES, PLC; BATUS HOLDINGS, INC.; BROWN & WILLIAMSON TOBACCO CORPORATION; PHILIP MORRIS COMPANIES, INC.; PHILIP MORRIS INCORPORATED (PHILIP MORRIS U.S.A.); LOEWS CORPORATION; LORILLARD TOBACCO COMPANY; UNITED STATES TOBACCO COMPANY; UST INC.; THE COUNCIL FOR TOBACCO RESEARCH--U.S.A. INC. (SUCCESSOR TO TOBACCO INSTITUTE RESEARCH COMMITTEE); THE TOBACCO INSTITUTE, INC.; HILL & KNOWLTON, INC.; BRITISH AMERICAN TOBACCO CO., LTD.; and DOSAL TOBACCO CORP., INC.,

Defendants.

DEPOSITION OF: DAVID EUGENE TOWNSEND, Ph.D.

DATE: May 29, 1997

TIME: 9:02 AM

REPORTED BY: A. WILLIAM ROBERTS, JR., Registered Professional Reporter, CP, CM, CRR, CLVS

Computer-Aided Transcription By:

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51676 0001

LOCATION: Adams Mark Hotel
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Winston-Salem, NC

TAKEN BY: Counsel for the Plaintiffs

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and

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In-House Counsel

ALSO PRESENT:

Christopher Cassler, Videographer

(INDEX AT REAR OF TRANSCRIPT)

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A. WILLIAM ROBERTS, JR. & ASSOCIATES

(PLF. EXH. 1, Plaintiffs' Notice of Video Deposition Duces Tecum, was marked for identification.)

(PLF. EXH. 2, Florida Rules of Civil Procedure deposition rules, was marked for identification.)

(PLF. EXH. 3, Rule 26 Expert Statement, was marked for identification.)

THE VIDEOGRAPHER: Okay, my name is Christopher Cassler, and I'm the videographer for Legal Video Services, and I'll be taping this proceeding. This is the deposition of David Townsend in the case of The State of Florida, I believe; is that correct?

MR. WESTBROOK: Correct.

THE VIDEOGRAPHER: The State of Florida versus American Tobacco Company. This deposition is being taken at Adams Mark Hotel located at 425 North Cherry Street in Winston-Salem, North Carolina. This is the beginning of tape 1. The date is May 29th, 1997, and the time is 9:02 AM.

MR. WESTBROOK: I think we should introduce ourselves for the record. My name is Edward Westbrook from the Ness, Motley firm. I represent The State of Florida.

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MS. FLOWERS: I'm Jodi Flowers from the Ness, Motley firm, and I represent The State of Florida.

MR. McDERMOTT: I'm Robert McDermott from Jones, Day. I represent R. J. Reynolds Tobacco Company and the witness.

MR. WEBER: And I'm Bob Weber from Jones, Day with the same representation.

MR. WESTBROOK: Swear the witness, please.

DAVID EUGENE TOWNSEND, Ph.D.

Being first duly sworn, testified as follows:

THE COURT REPORTER: State your full name for the record, please.

THE WITNESS: My name is David Eugene Townsend.

THE COURT REPORTER: Thank you.

MR. WESTBROOK: We have premarked before we went on the tape three preliminary exhibits:

Exhibit 1 is the notice of deposition in this matter.

Exhibit 2 is a copy of the relevant section of the Florida Rules of Civil Procedure, in particular Rule 1.310, governing the conduct of depositions upon oral examination. And this

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deposition will be governed by the Florida Rules of Civil Procedure. Including specifically with respect to deposition conduct, I quote:

Any objection during a deposition shall be stated concisely and in a nonargumentative and nonsuggestive manner. A party may instruct a deponent not to answer only when necessary to preserve a privilege, to enforce a limitation on evidence directed by the Court, or to present a motion under subdivision (d). Otherwise, evidence objected to shall be taken subject to the objections, unquote.

And exhibit 3 is the expert disclosure statement under Rule 26, provided by Dr. Townsend in this case.

We will offer those three exhibits and introduce those at this time.

EXAMINATION

BY MR. WESTBROOK:

Q. Doctor, let me hand you exhibit 1, which is the notice of deposition in this case.

Have you brought any documents, sir, in response to the request for documents?

A. I don't have any documents with me.

Q. All right. We were previously provided

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by your counsel with some sets of documents as reliance materials.

Do I understand, sir, that you have nothing further other than what counsel may have provided to us?

A. That's correct.

Q. Doctor, would you take a look at exhibit 3, which is the expert disclosure statement for you as provided to us by counsel for R. J. Reynolds.

Can you confirm, sir, that that's a current disclosure statement as you understand it in this case?

A. That is a current disclosure statement.

Q. All right. And attached to the disclosure statement is your current CV, sir?

A. That's right.

Q. Doctor, as we mentioned during the introductions, my name is Ed Westbrook, and I represent The State of Florida.

Do you understand, sir, that The State of Florida is suing your company for money damages?

A. I understand that.

Q. Okay. And I'm going to ask you some questions today, and I understand you've had your deposition taken before in some tobacco cases; is

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that right?

A. I've had several depositions, yes.

Q. All right. So you understand that if you don't understand the question, please ask me to rephrase it, and I will try to do so?

A. Right.

Q. Okay. Doctor, how old are you?

A. 49.

Q. And am I correct, sir, that for the last approximately 20 years, you've worked for R. J. Reynolds?

A. It's been 20 years this year.

Q. And during that time, have you been involved almost exclusively in cigarette design?

A. That's been the substance of my job for the entire 20 years.

Q. Have you worked anywhere else for the past 20 years at all?

A. No.

Q. Do you owe your livelihood, your current livelihood, to R. J. Reynolds?

A. That's my only employer, so I assume that's what you mean.

Q. And do you consider yourself as owing your loyalty to R. J. Reynolds in this matter?

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A. I certainly am loyal to my company. I am a scientist first, and I happen to be an employee of Reynolds second.

Q. We're sitting here in a hotel in Winston-Salem. Do you work here in Winston-Salem, sir?

A. I do.

Q. Okay. Currently, what is your position at R. J. Reynolds?

A. Currently, I'm Director of Product Development and Assessment in the Research and Development Department.

Q. All right. Now, by product development, do you work on the development of any products other than cigarettes?

A. No. All my work is focused on cigarettes.

Q. Okay. Are you currently married, sir?

A. I'm married.

Q. All right. Do you have children?

A. I have two daughters.

Q. And how old are they, sir?

A. The oldest is 24. The youngest is 20.

Q. Have you ever smoked cigarettes, sir?

A. Yes, I'm a current smoker.

Q. All right. Have you smoked cigarettes during the entire time you've been employed with R. J. Reynolds?

A. Yes.

Q. What brand do you smoke?

A. Right now I smoke Salem Ultra Light.

Q. And how many packs of cigarettes a day do you smoke?

A. That varies a lot, depending on what I'm doing during the day. I would say typically I smoke between a pack and a pack and a half a day.

Q. Have you ever tried to quit smoking, sir?

A. No.

Q. I take it, sir, you are not convinced that smoking is hazardous to your health, are you?

A. I don't think that's a fair assessment of my -- my opinion. I believe that cigarette smoking is certainly related -- it's a risk factor for certain diseases, and I don't know whether cigarette smoking causes those diseases. It may.

Q. And you've been working in cigarette design for 20 years, sir; and based on what you know, you've decided to continue smoking?

A. That's correct. I make the choice to continue smoking.

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DAVID E. TOWNSEND, Ph.D. - EX. BY MR. WESTBROOK

Q. Okay. And when you get up in the beginning of the day, sir, when do you have your first cigarette?

A. Generally after breakfast, after I have my first cup of coffee and when I'm in the car on the way to work.

Q. Okay. Do you smoke during meals?

A. During meals?

Q. Yes, sir.

A. Generally after a meal.

Q. Do you smoke in your home?

A. Yes.

Q. Does your wife smoke?

A. No, she doesn't.

Q. Do your daughters live with you in the home?

A. My oldest daughter has been living with us for the last several months but is getting ready to move out again.

Q. Okay. When your children were young and in the home, sir, did you smoke around them?

A. Yes, I did, some.

Q. All right. Do either of your two daughters smoke?

A. My oldest daughter smokes. My youngest

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daughter, I'm not quite sure. She may be an occasional smoker. It's hard for me to tell.

Q. Do you believe, sir, that your example of smoking around your children while they were young and letting them see you smoke over the years influenced their decision to smoke in any way?

A. I don't know to what degree my smoking may have influenced their smoking. I really don't know.

Q. Have you ever counseled either of your two daughters not to smoke?

A. When they were young, we've had several discussions about smoking. They've obviously asked me what I do at work and a variety of questions and that leads into the whole issue of smoking. We've had discussions about them not smoking and not being allowed or permitted to smoke when they were under age.

Q. When did your first daughter who began to smoke, when did she smoke?

A. I'm really not sure. I think it was while she was in college.

Q. Have you ever discussed with her whether she smoked without your knowledge at a younger age?

A. I can't remember that discussion, no.

Q. Okay. Did you ever smoke around your wife while she was pregnant, sir?

A. I don't believe I did. When my wife was pregnant with either of our children, I didn't tend to smoke in the home. I would go outside or at work.

Q. Okay. Did you make a conscious decision to avoid smoking around your wife when she was pregnant?

A. I made a conscious decision to avoid smoking around my wife because she didn't like the smell of it.

Q. Okay. After your wife's pregnancies had concluded, did you ever smoke around her in the house?

A. Yes. Off and on I've smoked in the house and presently I smoke in the house.

Q. Okay. When did you change your policy of not smoking around her because she didn't like it?

A. Well, I can't remember.

Q. Do you smoke in your office at R. J. Reynolds?

A. Yes, I do.

Q. Do you sit in the smoking section of restaurants when you go out to eat?

A. Sometimes. Sometimes if a restaurant is

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particularly full, I'll take the first available.

Q. Okay. Do you know anyone who works with you at R. J. Reynolds who is an antismoking advocate?

A. By antismoking advocate, you mean what?

Q. Someone who goes around and says, you know, Dave, you shouldn't be smoking; it's bad for your health. Why don't you give it up?

A. No, I'm not aware of a person who has that approach to smoking. I believe we have a number of scientists at Reynolds that I work with who do serious research into cigarettes, cigarette smoke. I think they're open-minded scientists, not biased advocates on either side.

Q. Do you believe that anyone who thinks that an individual should give up smoking is a biased advocate?

A. I think people make their own decisions about cigarette smoking and whether or not they or other people should smoke. That's clearly their decision to make.

Q. Have you ever counseled anyone either in your family or elsewhere that they should not smoke?

A. I have told my children that I would not allow them to smoke when they were under age.

Q. You would not allow them to smoke in the

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house?

A. I would not allow them to smoke, period.

Q. That is, of course, if you knew they were smoking, you would try to do something about it?

A. Right. That's right.

Q. All right. I take it, sir, that you would object to any company that advertised and tried to attract underaged smokers to use cigarettes?

A. Absolutely.

Q. Okay. And you are familiar with the Joe Camel ad campaign?

A. I'm familiar with parts of the campaign, yes.

Q. Are you aware that just in the last day or so, the FTC has announced action against your company concerning the Joe Camel ad campaign?

A. I'm aware of that. I haven't read the Complaint yet.

Q. Okay. Were you involved in the Joe Camel ad campaign, its formulation or whether it would attract children to smoke?

A. I was not involved at all in the formulation of the Joe Camel campaign.

Q. Sir, have you ever used any illegal drug?

A. No.

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Q. Have you ever been a party to a lawsuit?
A. No.
Q. Do you own any stock in R. J. Reynolds currently?
A. Yes, I do, a little bit.
Q. Do you own any stock in any other tobacco company?
A. I have a little bit of stock in Philip Morris.
Q. Does R. J. Reynolds ever give cigarettes to its employees without charge?
A. No.
Q. Do you ever take part in programs to smoke experimental or prototype cigarettes?
A. By a program of that sort, you mean what?
Q. Well, where somebody calls down to your office and says, Dr. Townsend, we've got a cigarette, X 1 we're trying out; would you like to take a pack home and smoke out. Do you do anything like that?
A. Okay. So you mean an experimental taste evaluation?
Q. If that terms suits you, yes, sir.
A. Yeah, I participate in some of those from time to time, sure.

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Q. And what is your role in the experimental taste evaluation? Is it to give your view on the taste, or are you in there for some other purpose?

A. No. Solely for the taste. We -- if we develop prototypes, we sometimes will have volunteer employees smoke those products, particularly employees who are particularly good at discriminating among various taste signatures of various products. We get their responses on the attributes of those products in a ballot form.

The experimenter then will compile the results of those ballots and make some judgment about whether this is a viable prototype or not.

Q. Doctor, I'm aware that you've testified in some depositions in a few trials over the past few years.

Can you give me an estimate of how much of your time is spent testifying or preparing to testify and how much is spent on other R. J. Reynolds activities?

A. That's hard to gauge. Certainly over the last couple of months, there seems to be a lot of litigation activity, and I think probably if I had to guess, the peak of this activity here, I'm spending maybe 15 or 20 percent of my time.

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Q. And I assume that you were chosen by someone within R. J. Reynolds to be a company spokesman on issues such as cigarette design in the tobacco litigation; is that correct?

A. I was -- I was -- I'm not sure chosen is the correct word. I was talked to by one of my former supervisors because that supervisor believed that I knew a lot about cigarette design.

Q. Okay. And who was that former supervisor?

A. Alan Rodgman.

Q. And about when was that that Dr. Rodgman approached you?

A. I really can't recall. It's been a number of years ago.

Q. Would you say it's been as many as five years ago?

A. I think that's fair, or perhaps longer. I really can't recall. It was quite a while ago.

Q. All right. What was your first -- I'll call it for want of a better term -- public appearance on behalf of R. J. Reynolds to speak publicly before a congressional body, a government body or any court body on matters involving cigarettes?

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A. A congressional body, Court body or what?

Q. Regulatory body, congressional body or in court.

A. Maybe I can give you just sort of a summary of some things. I'm not sure exactly when the first time was. I was heavily involved in the cigarette fire safety issue. And as a scientist participating in that effort, we worked with -- I worked with various members of the government, particularly through the National Institute of Standards and Technology, The Consumer Product Safety Commission.

So we had a number -- I had a number of interactions with those bodies, particularly The Consumer Product Safety Commission, to try to determine cigarette design characteristics and how they may affect fire safety. There have been -- and that was probably the earliest time I had contact with any regulatory or government bodies.

Q. And can you recall, sir, approximately when you first had contact with a government or regulatory body connected with matters involving smoking, cigarette design, and health matters?

A. I'm not sure I have been connected with a

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regulatory body concerning cigarette smoking and health matters.

Q. Do you understand, sir, that The State of Florida is suing your company to recover the costs that the state claims it has incurred because people have gotten sick from R. J. Reynolds' cigarettes?

A. I have a very superficial understanding of what The State of Florida's Complaint is, but I understand it's, in layman's terms, if you will, it's to try to recover Medicaid costs.

Q. Okay. In connection with costs spent on health concerns?

A. I think that's a fair characterization.

Q. All right. In preparing to appear before regulatory bodies, did you receive any training at R. J. Reynolds as to how you should conduct yourself, or how you should speak, act, appear?

A. No. My presentations to regulatory bodies in the fire safe cigarette issue, for example, was scientific. I made a number of scientific presentations to those bodies. We discussed scientific issues. And, frankly, that's my training.

As a result of some of the cigarette fire safety questions, R. J. Reynolds expected some media

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attention, so I did receive one or possibly two fairly brief media training sessions that centered around the cigarette fire safety issue.

Q. All right. Have you ever been a spokesman for R. J. Reynolds at a press conference or on camera, before a TV camera?

A. I was a spokesperson for R. J. Reynolds -- you mean to the media?

Q. Yeah. You said there was some expected media attention, and I'm wondering, were you an R. J. Reynolds spokesman, someone who comes out of the office door and gives R. J. Reynolds' position on the steps of the office?

A. I have given press interviews on the cigarette fire safety issue. There have been several, both local -- local television as well as national television.

Q. Where were these media training sessions conducted?

A. As I recall, there was a brief training session in New York, and then I think there was a very brief follow-up one afternoon sometime later here in Winston-Salem.

Q. Did you go to New York for the purpose of attending a media training session?

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A. Yes.

Q. Do you know a Dr. Christopher Coggins who used to work at RJR?

A. Yes, I do know him.

Q. All right. Was Dr. Coggins involved in the media training session you attended?

A. I can't recall ever being on a business trip with Dr. Coggins. I think this question came up in the Connor trial, and I've thought about it, and I can't recall ever being on a business trip, much less in New York on media training, with Dr. Coggins.

Q. Tell me about the media training. What did you do there?

A. Mostly -- well, there were, I guess, two major phases to the media training. One was instruction on kind of what the media is looking for, how to boil down sometimes a complex piece of information to something that the media will understand and can use. That's particularly difficult to trained scientists like myself, because we tend to think about all the complexities. It's hard to get those kind of -- those kind of technical issues across to the media. So the first part was largely instruction.

The second part was role playing, where

we actually in front of a camera would go through mock questions.

Q. And did you then review the videotape of your own performance on the camera?

A. Yes, and it wasn't pretty.

Q. It's like a lawyer reading a deposition transcript for the first time; it doesn't sound the way you thought it sounded.

A. That's right.

Q. Am I correct that you had this session and then one other follow-up session with the media consultants?

A. As I can recall, those were the only two sessions we had. The second session was here in Winston-Salem, and it was I think just an afternoon of role playing, again mock questions.

Q. All right. Did you get advice from the media consultants on how you should dress when you are making an appearance on behalf of R. J. Reynolds?

A. I can't recall that, no.

Q. Do you recall getting instructions on how you should conduct yourself, what your demeanor should be?

A. I think in the instruction phase there was something about demeanor, about trying to

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carefully understand the question, try to deal with the reporter directly face-to-face. I think there was some instruction about that. I can't recall the details.

Q. All right. Was the session in New York that you talked about, the first session, conducted by an outside media consultant?

A. Yes.

Q. Who was that consultant?

A. The media consultant was Virgil Scutter.

Q. Did you take any of the videotapes of your own performance during this first session in New York home for review?

A. No, I don't think so.

Q. Do you know where those tapes are today?

A. (Moves head from side to side.)

Q. Approximately when did you have the initial media training session in New York?

A. It's really hard for me to recall exactly at this time. I would say it was in the late '80s. '88, '89, thereabouts.

Q. All right. Let's talk about your testimonial appearances in court proceedings.

Did you have any training other than these two media sessions on how you should conduct

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yourselves -- yourself in a courtroom?

MR. McDERMOTT: Object to the form of the question. You are assuming facts not in evidence. The media training pertained to his earlier work and had nothing to do with courtroom appearances. That's not a fair question.

THE WITNESS: The media training I did attend was centered on cigarette fire safety, and I've not had any media training or any training about, as I can recall, about how to behave in litigation, for example.

BY MR. WESTBROOK:

Q. All right. Doctor, I don't want to know what you have discussed with attorneys in preparation for testifying, but I want to ask you, have you prior to testifying in trial in tobacco health cases, such as someone suing your company because they claim to be sick, have you met and prepared your testimony with attorneys?

A. Yes. I've had a number of meetings with attorneys.

Q. Are those including attorneys that work outside R. J. Reynolds?

A. That work outside? What do you mean?

Q. Who work outside R. J. Reynolds.

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A. Who are not employees of R. J. Reynolds?

Q. Yes, sir.

A. Yes.

Q. Okay. Doctor, in your approximately 20 years at R. J. Reynolds working on cigarette design, has R. J. Reynolds developed a cigarette that in your view will not cause any disease to someone who smokes it on a regular basis such as one pack a day for 20 years?

A. I don't know. We've made a lot of progress developing cigarette -- cigarettes that have substantially reduced chemistry and have reductions in some biological assays. Whether that will reduce diseases that are thought to be associated with cigarettes, I don't know.

See, there is no way to prove whether -- whether one cigarette is really safer than another. But we do have substantial reductions in chemistry and some reductions in biology.

Q. If I were to take a high tar cigarette, put it on a table next to a low tar cigarette, light or ultra light, however you want to call it, would it be your view, sir, that you can't say whether the high tar cigarette is more dangerous than the low tar cigarette?

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A. I think, again --

MR. McDERMOTT: Just a moment. Go ahead.

THE WITNESS: I think, again, there is no way to prove whether one cigarette is safer than another. I think if cigarettes are a risk for certain diseases like lung cancer, then the expectation is that less exposure would be better.

So to me, the expectation is that an ultra low tar product should be better than a high tar product, but there is no way to prove that.

BY MR. WESTBROOK:

Q. Now, is R. J. Reynolds' leading brand of cigarettes Winston?

A. The leading brand family right now is Doral.

Q. Doral? Does that mean Doral is R. J. Reynolds' biggest seller right now?

A. As a brand family, that's correct.

Q. How about an individual cigarette type that is within a brand family, what is R. J. Reynolds' biggest selling cigarette?

A. I believe that's still Winston.

Q. Can you tell the Court and the ladies and gentlemen of the jury that if someone smokes Winston

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one pack a day for 20 years that that person can be assured of not getting a disease?

A. No, I can't -- I can't tell a person that. I have no way of knowing whether a person is going to get a disease or not any more than anybody else can.

Q. Over the years, Doctor, I assume you've worked on a number of different products -- projects involved in cigarette design; is that right?

A. That's correct.

Q. Okay. Have you published the results of any of your cigarette design projects in the peer reviewed scientific literature?

A. Published the results of cigarette design projects?

Q. Yes, in peer reviewed scientific literature.

A. You mean new product development?

Q. Well, new product development or some other work you've done on cigarette design in peer reviewed scientific literature.

A. Are you talking about me personally or my company?

Q. Yes, you personally.

A. No, I have not personally.

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Q. What is the last article you recall publishing on cigarette design in any scientific literature, peer reviewed or not?

A. I actually haven't published very much. I have about three or four papers relating to cigarette fire safety from my stay at Reynolds. Most of the work that I do is highly proprietary. It is product development and is proprietary information.

Q. Doctor, let's talk a little bit about cigarette design matters, which I understand is your field.

I think we can agree, Doctor, that cigarettes are not just chopped up tobacco rolled in paper; is that right?

A. I'm not sure where you're headed with that, what your question is.

Q. You don't need to worry about where I'm headed. Can we agree on that?

A. Sure.

Q. Okay.

A. Can you ask the question again because I'm not sure.

Q. Yes, sir. Can we agree, Doctor, that cigarettes are not just chopped up tobacco rolled up in a piece of paper?

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A. I think by definition, cigarettes -- cigarettes by the government's definition are tobacco rolled in paper. I think it's clear that modern cigarettes today have evolved over a number of years, and it's -- to produce a modern cigarette requires a lot of technical expertise in blending, in engineering cigarette papers, filters, air dilution and a number of design parameters.

Q. Let's talk about the cigarette itself. To produce a modern cigarette today, you don't have to put any additives in the tobacco, do you?

A. Most cigarettes in the U. S., almost all cigarettes in the U. S., have additives or flavors of one sort or another. It's not absolutely essential.

Q. And is it true, Doctor, that quite recently, R. J. Reynolds has introduced a cigarette that advertises it has no additives?

A. We have a Winston product that's been in test market in Florida that has no additives added by the manufacturer.

Q. All right. And has that product been a success?

A. I think it's done well in Florida, yes.

Q. And has it been so successful that R. J. Reynolds, in fact, intends to market it

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nationally now?

A. That's our plan.

Q. You intend to come out in July with it on a national basis?

A. That's our plan.

Q. Okay. So at least in the case of Winston, I think you call it No Bull; is that right?

A. Well, I'm not a marketing expert. I'm not quite sure where that came from but that is one of the tag lines.

Q. All right. At least in the case of Winston No Bull, additives don't seem to be necessary for public acceptance of a cigarette, do they?

A. We've been able to design and build that product so that it is an acceptable product without flavors and additives.

MR. WESTBROOK: Let's mark as next a package of Winston Filters, which will be 4, and as exhibit 5 a package of Salem cigarettes.

(PLF. EXH. 4, One pack of Winston Filters cigarettes, was marked for identification.)

(PLF. EXH. 5, One pack of Salem cigarettes, was marked for identification.)

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BY MR. WESTBROOK:

Q. Doctor, as you well know, any time you need a break, just let me know, and we'll stop.

(Off-the-record conference.)

BY MR. WESTBROOK:

Q. Doctor, let me hand you what we've marked as Plaintiffs' Exhibit 4, a pack of Winston cigarettes, and ask you to hold those up for the camera, if you would, please, sir.

A. (Complying)

Q. Do you recognize those as an R. J. Reynolds products?

A. Winston Filters is an RJR product.

Q. All right. And you've been involved in cigarette design for 20 years at Reynolds. Sir, with that background, can you tell me what are the additives in that pack of Winston Filters?

A. The flavors that are in this particular pack of Winstons is a proprietary secret and proprietary information.

Q. If I'm a Winston smoker, sir, and I want to know what additives -- now that I've heard about additives -- what additives are in that tobacco, can I call up a hot line or toll line or something at Winston and get that information?

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A. Not for this brand specifically. You can get information on additives that are used in the industry in the U. S. That's public information.

Q. What if I want to know what's in the cigarettes that I smoke, and I call up, and I happen to get you on the line at R. J. Reynolds, and I ask you, Dr. Townsend, I understand you know 20 years worth of information about cigarette design; what additives are in the Winstons I smoke? Would you tell that person?

A. That's proprietary information.

Q. So you wouldn't tell that person?

A. I would not tell that person.

Q. All right. Let me hand you exhibit 5, which is a pack of Salems. Would you hold that up for the camera, sir.

A. (Complying)

Q. All right. Do you recognize those Salems as a product of the R. J. Reynolds Company?

A. Yes, I do.

Q. All right. Is that the brand line that you smoke? I know you don't smoke that particular type but that's the brand line you smoke, Salems?

A. That's the brand family I smoke.

Q. Thank you, sir. And, again, if I were to

51676 0033

call up R. J. Reynolds, is there anyone at Reynolds who will tell me what additives are in those Salem cigarettes?

A. Again, that's proprietary information.

Q. As you sit here today, Doctor, do you know what's in those cigarettes by way of additives?

A. Many of the flavors that we use in our products are not only proprietary for RJR, but they are proprietary for some of our suppliers. We have toxicologists in our Research and Development Department that know the intimate details of all our flavors and additives, but scientists such as myself who don't have a need to know do not know the details, not all of the details.

Q. All right. So when you smoke a Salem Light or Ultra Light, whichever you smoke, am I correct that you don't know all of the additives that are in the cigarettes you are smoking?

A. That's correct.

Q. Have you heard of something called GRAS, G-R-A-S, with respect to additives?

A. Yes, I have.

Q. What does GRAS mean?

A. GRAS is an acronym for generally regarded as safe.

51676 0034

Q. Have you heard of another acronym called FEMA, F-E-M-A?
A. Yeah, I have. And I'm not quite sure what that stands for. I'm not an expert in this area.
Q. Okay. Have you seen the term FEMA GRAS used with respect to additives?
A. Yes.
Q. Okay. Do you understand what that term means?
A. No.
Q. Let me mark as next the industry's 1994 generic disclosures of additives, and I'm going to ask you some questions about it.
(PLF. EXH. 6, UPI article with attached April 12, 1994 document entitled Ingredients Added to Tobacco in the Manufacture of Cigarettes by the Six Major American Cigarette Companies, was marked for identification.)
BY MR. WESTBROOK:
Q. Doctor, let me hand you what we've marked as exhibit 6, which is the press release concerning the tobacco industry and mentioning R. J. Reynolds and the industry's April 12th, 1994 generic additives

51676 0035

list, and I'll ask you to take a few minutes to review the press release in particular, and then I'm going to ask you some questions about that. And also if you want to flip through the additives list and confirm that that is the list of additives that was released in 1994.

MR. McDERMOTT: While the witness is reviewing this, and just so that the record is straight, I believe you indicated that this was a press release. It appears that this is a UPI report. I'm not sure if you have different information than I do, but it appears that it is a publicly generated story rather than an industry statement as such.

MR. WESTBROOK: That is a very valid clarification, and I appreciate that. That's what I meant. Press release is a misnomer. It is a newspaper article concerning the release.

MR. McDERMOTT: If you want the witness to review the entire list, does it make sense to turn off the camera and let him do that?

THE VIDEOGRAPHER: Do you want to go off the video?

THE WITNESS: Do I need to review the entire list or scan it or --

51676 0036

BY MR. WESTBROOK:

Q. You don't. I don't think we are going to discuss it in too much detail. We may look at a few, but I think I really wanted you to look at it and confirm that that seems to be a list in the form and content of the 599 additives that were released in 1994.

A. Okay, I've scanned the news release or the news document.

Q. Okay. Doctor, do you recall about the time that the industry released the additives list in 1994? Do you remember that happening?

A. I recall that time, yes.

Q. All right. And do you recall that the industry released a generic list that combined all their additives into one list and didn't specifically identify which additive was in which cigarette?

A. That's correct.

Q. Okay. The newspaper story that's attached to the list states that R. J. Reynolds revealed the ingredients on behalf of the major U. S. cigarette manufacturers.

Are you familiar with the fact that Reynolds was the company that released the generic list on behalf of all the companies?

51676 0037

A. I'm not sure of the details of how that actually occurred.

Q. There is a Reynolds spokesman, David Fishel, F-I-S-H-E-L, mentioned. Do you know Mr. Fishel?

A. I know Mr. Fishel.

Q. Is he in the Public Relations Department of RJR?

A. Yes.

Q. Now, Doctor, if we can, would you turn to the first page of the list itself and let's look at the very first additive.

Are you familiar with that additive, sir, the name of that additive?

A. I've -- I've heard of this before. I'm not familiar with what it is, though.

Q. All right. As I pronounce it, it's Acetanisole, but that's probably not correct.

A. I would say Acetanisole.

Q. Acetanisole. All right. And Acetanisole is listed as being an FDA-approved food additive, correct?

A. That's what it says.

Q. All right. Does it say anywhere that this additive is approved by the FDA for use in

51676 0038

tobacco?

A. Let me read the whole thing. Acetanisole, FDA-approved food additive; FEMA GRAS; found in beef, cranberry, guava, grape, mango, peppermint; used in frozen dairy products and hard candies.

Q. All right. Does it say anywhere on the industry-released list that Acetanisole has been approved for use in cigarettes?

A. It does not say that.

Q. All right. And with reference to the FDA approval for food, is it correct that your company, R. J. Reynolds, is fighting FDA regulation of its cigarette business?

A. My company does not agree in general that FDA regulation makes sense.

Q. So is it correct that your company is fighting FDA regulation of its cigarette business?

A. That historically has been in essence the position. I think we're all aware that there are talks now going on about potential regulation and potential settlement. I don't know the details of that frankly.

Q. All right. You've anticipated something I was going to ask you much later. I take it that

51676 0039

you have not been involved at all in formulating R. J. Reynolds' position on whether to acquiesce in any type of regulation by the FDA or whether to settle any lawsuits; is that right?

A. Not at all.

Q. Okay. Now, the word FEMA GRAS appears here under Acetanisole, and we discussed that previously.

Does a FEMA GRAS rating in your opinion or knowledge relate to tobacco at all?

A. We're in an area that I'm really not an expert in. I know that many of our toxicologists who do worry about additives and know the details of all the additives that we use in our products do look at a variety of information about a particular additive. Whether they are approved for food use, whether they are GRAS, whether they are FEMA, they also do their own toxicological testing to ensure that the use of that additive doesn't increase the biological burden of the cigarette.

Those tests may include pyrolysis studies where they look at compounds that may be produced on burning that material. It may include a variety of biological end points. It certainly includes thorough monitoring of all scientific literature that

51676 0040

may deal with that additive.

Q. All right. Is it your understanding, sir, that R. J. Reynolds has done pyrolysis testing on each additive that is used in its cigarettes?

A. That's not my understanding, and I don't think I said that.

Q. I think you said may. That's why I asked you.

A. Yeah. I think our scientists look at what's in the literature about a particular compound, understand thoroughly what is in the literature, and based on that, plus expectations from their toxicological expertise, decide what tests are appropriate. Those tests may be a certain set of biological end points. They may be pyrolysis.

But the particular experiments that are conducted depend on that compound, what's expected behavior of that compound, what expected decomposition products might arise from that compound as well as from the bulk of the scientific literature.

So it depends on which compound you are talking about.

Q. Now, the industry list, and again, referring to Acetanisole, has as the first reference

51676 0041

that it's an FDA-approved food additive.

What difference does that make on a cigarette additive list? Why did the company put that in?

A. Again, I'm not an expert in this area, but I think our toxicologists look at all the available information. The fact that it's an approved food additive in and of itself I think is not the only information. They certainly look at that plus the fact that it's FEMA, plus GRAS, plus all the scientific literature, everything that's known about Acetanisole and may even do our own biological studies.

Q. Let's talk a little bit about the FEMA GRAS situation.

MR. WESTBROOK: Let's mark as next the FEMA GRAS list for GRAS substances. This one is dated 1965. This will be exhibit 7?

THE COURT REPORTER: Yes.

MR. McDERMOTT: Let me interpose an objection here. You may consider it a foundation objection. The witness has already indicated he does not have expertise in this area. If this is how you choose to use your time, I'm not going to instruct him not to answer, but the witness has already

51676 0042

indicated he is not intimately familiar with this program and is not involved personally in the evaluation and testing of additives; but if you wish to pursue this, be my guest.

MR. WESTBROOK: I won't take a lot of our time responding, except to say as director of product development, the witness certainly has some familiarity or should have some familiarity of what goes into the products his group is developing, but I won't belabor the record with that.

(PLF. EXH. 7, Document entitled "Recent Progress in the Consideration of Flavoring Ingredients Under the Food Additives Amendment, III. GRAS Substances", was marked for identification.)

BY MR. WESTBROOK:

Q. Doctor, let me hand you the 1965 listing from the Flavoring Extract Manufacturers' Association, commonly known as FEMA, called GRAS Substances and ask you, sir, to take a look at that. And I'm particularly going to ask you about the table for each of the substances that's attached, and I'm going to ask you some general questions.

Please take a look at it and take

51676 0043

whatever time you need to look at it.

A. Well, I've scanned the first several pages very quickly and just glanced at the table.

Q. All right. In light of your counsel's comments, sir, let me ask you how things operate there in your cigarette design department.

Do you have people who work under you who are responsible for giving input to your group on the additives that are going to be used in the cigarettes that the design group is making?

A. My product -- my product developers work directly with flavor experts who are in a separate group. Those flavor experts work closely with flavor suppliers as well as with their own flavor research people and recommend certain types of flavors that may be candidates for new products or for changes to existing products.

Q. All right. In common parlance, are you the boss of the people who are looking at the additive questions in cigarette design?

A. No.

Q. Okay.

A. I'm responsible for product development. My product developers work directly with the flavor researchers and the flavor developers who are in a

51676 0044

separate group. Now, the other group of people that we've not really talked about very much is the toxicology group who are in a yet separate group who also work hand in hand with my developers and also with the flavor researchers.

Q. I guess my question wasn't clear. Do I understand that there are people under you who work under you who get the information on additives from others within your company?

A. No.

Q. Okay. Well, who decides whether an additive goes in a cigarette that Reynolds is going to develop?

A. This -- this is -- this is actually very easy if you'll let me back up.

Q. Let's back up.

A. We have three groups that work very closely in developing new products with respect to this one issue, additives. The product developers that work in my group work very closely with the flavor researchers who suggest particular flavor materials that may be best for a particular new product.

All at the same time, toxicologists from our Scientific and Regulatory Affairs Department also

within Research and Development are constantly working with the flavor researchers and with my product developers, and it's the toxicologists who understand all of the compounds, all of the constituents that are in these flavor packages. They understand the toxicology.

They decide and direct whether or not biological testing or pyrolysis testing or additional chemistry testing is required to ensure that the additives that we use in our product development don't increase biological end points.

Q. Okay. So your Product Development Group of which you are head works closely with the toxicologists?

A. With the toxicologists and the flavor research people.

Q. Okay. So the three groups work very closely together?

A. Absolutely.

Q. Okay. Are you aware, sir, of whether or not Reynolds is a member of FEMA itself?

A. I don't know.

Q. Now, with respect to FEMA GRAS, sir, do you understand that those are substances that FEMA has analyzed and has issued a generally regarded as

51676 0046

safe rating for those substances?
A. That would be my superficial understanding of that.
Q. Okay. Well, today is not the first day that you've heard the term FEMA GRAS, is it?
A. No, of course, not.
Q. Okay.
A. But, again, I don't understand the details of what goes on there.
Q. Okay. Looking at the industry list for Acetanisole, after FDA-approved food additive is the word FEMA GRAS.
Did you see the list in 1994 when it came out, that is, the additive list?
A. I'm sorry, your question is did I see the 1994 list when it came out?
Q. Yes, sir.
A. Yes, I did.
Q. Okay. Did you look at it at all?
A. I briefly scanned it. Frankly, again, you know, I don't -- I don't know all of the additives that we at Reynolds use and how our additives are a subset of that entire package from the industry, the 599 compounds.
Q. Okay. Let me ask you this: If you have

51676 0047

this list in hand, and you are Dr. Townsend, cigarette designer, can you from this list then figure out which additives are in those Salem cigarettes that you are smoking?

A. No.

Q. Can you from this list define anywhere the additives that are in any cigarette brand being made in 1994?

A. If you're referring to the list in the previous exhibit --

Q. Yes, sir.

A. -- the 599 list --

Q. Yes, sir.

A. -- that is a compilation of all the additives that are used by the entire -- by all the tobacco companies in this industry in the U. S. It does not tell you what particular additives are used by one individual company or by one company in a specific brand.

However, as I said, you know, at R. J. Reynolds, we have toxicologists who understand all of the intimate details of the additives that are used in our products. They understand the scientific literature and do the appropriate biological chemistry and testing.

51676 0048

Q. All right. Where has this testing been published by R. J. Reynolds on R. J. Reynolds' additives?

A. What do you mean published?

Q. Well, if I want to go look at it and find the R. J. Reynolds' pyrolysis data on the additives used in RJR cigarettes, where can I find that in a medical school library?

A. This is proprietary information, and I don't think you'll find the evaluation of our additives published in peer reviewed or in medical journals.

MR. McDERMOTT: Ed, why don't you look for a place in the next few minutes where it will be convenient to break.

BY MR. WESTBROOK:

Q. All right. Doctor, let's look at the FEMA GRAS list for a minute, and since Acetanisole, which is the first additive that we've been talking about in the industry list, has a FEMA GRAS approval rating, could you tell me from the FEMA GRAS list where the category is for approval for use in cigarettes?

MR. McDERMOTT: Object. No foundation. You may answer.

51676 0049

THE WITNESS: If I look down the FEMA GRAS list, I find Acetanisole. It says there are 12 reports, and then it breaks those reports down into beverages, ice creams, candies, baked goods, nothing in gelatins or puddings, and in chewing gum.

BY MR. WESTBROOK:

Q. Okay. There is no tobacco report, is there?

A. No, there is not a category called tobacco.

Q. All right. Are you aware, sir, that FEMA takes the position that its GRAS listing is only for the categories of usage that has been tested?

MR. McDERMOTT: Object. No foundation.

THE WITNESS: I'm not an expert in this area. I don't know what FEMA has decided.

MR. WESTBROOK: Let's take a break.

THE VIDEOGRAPHER: Okay. We're going to go off the videotape record. The time is 9:54 AM.

(A recess transpired and Mr. Donahue arrived at the deposition.)

THE VIDEOGRAPHER: All right. Okay, we're going back on the videotape record. The time is 10:05 AM.

BY MR. WESTBROOK:

51676 0050

Q. Doctor, before the break, you mentioned that your group worked closely with the toxicologists at R. J. Reynolds; is that right?

A. That's correct, my product developers work hand in hand with the toxicology group in the Research and Development Department.

Q. Can you identify for me the toxicologists who have done pyrolysis testing on additives in R. J. Reynolds' cigarettes?

A. Again, if you understand my answer to the earlier question, the toxicologists review all the scientific information that's available in the literature, and they conduct a variety of different biological tests, some chemistry tests or pyrolysis studies.

The toxicologists direct that program, understand all the data and may actually direct chemists within the Research and Development Department who are outside of the toxicology group to collect additional chemistry information, or conduct pyrolysis studies using a pyroprobe with a mass kratometer to identify products, and chemists will conduct that.

Toxicologists won't conduct that experiment, for example, but they will lay out a

51676 0051

research program. The chemists will conduct that. The biologists will conduct the biology piece of it. The toxicologists then accumulate all the information and try to understand it.

Q. Okay. Identify for me, please, Doctor, the chemists and biologists working under the toxicologists who actually have conducted pyrolysis tests on additives used in R. J. Reynolds' cigarettes.

A. Pyrolysis experiments are conducted in the Analytical Department of R. J. Reynolds, and -- you're looking for an individual's name?

Q. Individual or individuals?

A. The primary researcher is Dr. Henry Chung, who is a specialist in pyrolysis -- well, he is actually a specialist in mass spectrometry.

Q. All right. And has Dr. Chung performed a pyrolysis testing on additives that are used in R. J. Reynolds' cigarettes?

A. He has performed pyrolysis studies to support the toxicologists -- the toxicology questions of the toxicology group.

Q. In connection with cigarettes?

A. In connection with cigarettes and cigarette additives.

51676 0052

Q. Okay. Do you know which additives he has performed pyrolysis testing on?

A. No, not off the top of my head.

Q. All right. We've used this term pyrolysis, Doctor. We better define it a bit.

As you use the term pyrolysis, what parameters do you put around pyrolysis testing for cigarettes? What are you trying to duplicate?

A. The main objective of these kinds of pyrolysis studies are to heat a particular compound at a very controlled rate, a very measurable rate, but one that is very quick and simulates to the best of our ability the fast heating temperatures that are observed in a cigarette and actually measure decomposition products that may result from that rapid heating.

Q. All right. What is the temperature at which a cigarette burns the tobacco and the additives?

A. That's a complicated question. There is actually two major areas in a burning cigarette. There is a pyrolysis region, and then there is a combustion region.

The combustion region is mainly the oxidation of carbonaceous char. That's the area that

you see sticking out the front end of the cigarette that's glowing red hot. That's mainly just a straight oxidation of char to generate mainly carbon dioxide, water, some carbon monoxide and a few other small compounds.

Q. What's the temperature there?

A. And the temperature in that region is -- in between puffs is around 800 degrees Celsius. During a puff that region can get up to 1,000 to 1200 degrees Celsius.

Q. And what would that convert to roughly to Fahrenheit for those people who are more familiar with Fahrenheit?

A. Well, 800 degrees Celsius would be about 1500 degrees Fahrenheit. Now, pyrolysis of tobacco and tobacco constituents, tobacco additives occurs in what we call the pyrolysis region, which is actually just inside the cigarette paper, at the front edge of the cigarette paper. The temperatures there are substantially lower because that's not where the char oxidation occurs.

In the pyrolysis region, that's where you would expect any additives to be pyrolyzed, temperatures there range from -- range up to about, oh, in the neighborhood of 3 to 400 degrees Celsius,

which would be roughly 700 degrees Fahrenheit.

Now, one of the difficulties in doing pyrolysis studies of this sort is that heating rates in a burning cigarette during a puff are extremely fast and extremely high heating rates. So heating rates can approach 4 to 500 degrees Celsius per second. It's very difficult to develop a pyrolysis study where you can heat in a controlled way in the laboratory an additive or any other compound at that high heating rate in a very reproducible fashion.

But with modern pyrolysis techniques, particularly with an apparatus called the pyroprobe, we can get close to that. So -- and then from -- to finish giving you a picture of what the experiment is, we, in a very controlled way, try to heat the sample at very high heating rates that as best as we can simulate those that might be occurring in a burning cigarette during a puff, and then we measure the materials that come off that sample, try to identify them by mass spectrometry to first identify those pyrolysis compounds, the decomposition products. And then once we've identified them, we try to estimate the levels of those decomposition products that come from that pyrolysis.

Q. All right. Can -- just to give me a

51676 0055

frame of reference, Doctor, are you familiar with the temperature at which, for instance, a steak cooks on a barbecue grill?

A. You are talking about the steak temperature itself?

Q. No. I guess the temperature at the surface of the steak/grill interface if you want to be scientific.

A. I have no idea what that is. I would assume it is pretty warm. Probably warmer for some than others.

Q. Would it get up to 700 degrees?

A. Celsius?

Q. Fahrenheit.

A. Fahrenheit? It might get very hot. I'm not sure it would get quite that hot, but particularly where there is physical contact between the steak and the grill, I would expect it to get very hot because of the -- you have conductive heat transfer where the steak actually physically touches the grill surface. Where it doesn't touch, then you have heating primarily by convective heat transfer, and the temperature should be somewhat lower.

Q. All right. When you say very hot, can you give me a ballpark? Are you talking about 3 or

51676 0056

400 degrees, or are you talking about close to 700 degrees?

A. I couldn't really guess. I would say it was -- well, I couldn't really guess without making measurements.

Q. Would you expect it to be as low as 2 or 300 degrees?

A. Well, if you're forcing me to guess, I would say it would be in the neighborhood of a couple hundred or 300 degrees or so as opposed to 7 or 800 degrees Fahrenheit, but that's just a guess.

Q. Would you agree with me, Doctor, that the temperature at which pyrolysis occurs in a cigarette is much higher than the temperature normally encountered in a home oven?

A. I think that's a broad generalization, because a compound will pyrolyze at whatever temperature that compound pyrolyzes. And many compounds will pyrolyze at low temperature. Many compounds will pyrolyze and decompose at a much higher temperature.

So I have a hard time making a sweeping generalization like that.

Q. But if I want to go home and try to duplicate what's happening in a cigarette and put

51676 0057

some probes in my oven at home and measure what the pyrolysis of products are in a cigarette, if I put the cigarette in the oven and turn it up to the normal baking temperature, 325 or 350 which I see on cake boxes, do you expect I will get the same results as your folks are getting back in their pyrolysis lab?

A. Can you rephrase that? I don't understand your question.

Q. Say I wanted to go home and conduct my own experiment on a Winston and see what the pyrolysis products are of the additives in tobacco. If I put that cigarette in a pan and put it in the oven at 350 degrees, the temperature at which my wife usually bakes a cake, do you expect I will get the same results as R. J. Reynolds gets when it conducts the pyrolysis experiments in its laboratory?

A. Well, again, I think this is a very complicated picture because some constituents in tobacco will decompose at low temperatures, even at temperatures 100 degrees or 150 degrees. And certainly in an oven at 3 or 400 degrees, there is going to be decomposition of some tobacco constituents and some additives.

Other additives won't decompose until a

much higher temperature, those that may be present in the pyrolysis region of a cigarette. So you will get one set of data from your oven experiment if you conduct it carefully, and that set of data can be replicated in the laboratory probably pretty well under those temperature conditions; but in your oven, of course, you won't see decomposition products that result from higher temperature decomposition mechanisms.

Q. Am I correct, sir, that your background is in chemistry?

A. That's correct.

Q. Okay. Do you have an understanding of what happens when sugar pyrolyzes at the temperature in a cigarette?

A. Yeah, I have a general understanding of it. I am certainly not an expert in carbohydrate chemistry.

Q. What are the products that are given off during the pyrolysis of sugar?

A. Well, there are a number of carbohydrate, in general, decomposition products. Acetaldehyde could be one, furans, furanes, a series of general classes of that sort.

Q. And what is acetaldehyde?

51676 0059

A. Acetaldehyde is a low molecular weight compound of a class that we call aldehydes.

Q. Does the substance have any danger to it?

A. I don't understand danger.

Q. All right. Is the substance hazardous to health at any levels?

A. Well, I'm not really an expert in that. I think my general knowledge from chemistry is that acetaldehyde is irritating. Whether it's a toxic compound or has any other toxic properties, I can't say right off the top. I would have to look it up.

Q. Are you familiar with a substance called aflatoxin?

A. Aflatoxin, I've heard of it, sure.

Q. What is it?

A. It's a compound that's thought to be highly toxic that is sometimes found in grains and ...

Q. Is it also sometimes found on stored tobacco?

A. Aflatoxin? I've never heard that.

Q. Do you know if R. J. Reynolds has any procedures to treat tobacco to reduce or prevent aflatoxin from growing on the leaf?

A. I've never -- I'm not aware of that.

51676 0060

I've never heard that there is any concern among growers or industry or anyone on aflatoxin contamination of tobacco.

Q. Are you aware if R. J. Reynolds does any testing of the tobacco leaves that it buys to see if they contain aflatoxin?

A. I am not aware of that, either.

Q. Are you aware of any testing that R. J. Reynolds has done in any of its laboratories to see if any aflatoxin survives or is present in cigarette smoke?

A. I'm not aware of any testing along those lines. I would say that aflatoxin probably is a very unstable material under heating. I would be surprised if there -- you know, if it would survive the heating process and actually be found in the smoke.

But, again, back to your question, I'm not aware of any specific experiments that have been done. I just don't know.

Q. Sir, without being specific as to brand, because I know you don't want to do that, in a general way, can you tell me, does R. J. Reynolds use any cocoa as an additive in any of its cigarettes?

A. Cocoa has been used in what we call the

51676 0061

casing formulations for cigarettes.

Q. All right. And by casing, do you distinguish that from an additive?

A. In -- within our company, we have casings, which are primarily sugars with some other flavorings, and then we have what are called top dressings, which are our primary flavor package additives.

The top dressings are generally extremely low levels. The casings ingredients, like sucrose or fructose, corn syrup, are at somewhat higher levels.

Q. And is cocoa a casing?

A. It has been used as a casing ingredient, yes, sir.

Q. Is it still used today?

A. Yes.

MR. WESTBROOK: Let's mark as next a document entitled National Cancer Institute Smoking and Health Program, The Third Set of Experimental Cigarettes.

(PLF. EXH. 8, Document entitled National Cancer Institute Smoking and Health Program, Report No. 3, Toward Less Hazardous Cigarettes, The Third Set of Experimental Cigarettes, was marked for

51676 0062

identification.)

THE COURT REPORTER: That's Plaintiffs' 8.

BY MR. WESTBROOK:

Q. Dr. Townsend, in response to our document request, we were provided with a number of documents that you may rely on in your direct testimony, and this document was one of them, sir.

Do you recognize the document?

A. Yes, I do.

Q. Okay. Did you participate in the National Cancer Institute program on looking toward less hazardous cigarettes?

A. Me personally?

Q. Yes, sir.

A. No, I didn't. I wasn't an employee of the company until after this actually was finished.

Q. The document is listed as one of your reliance materials and was provided to us, Doctor.

Have you read the materials that were provided to us as your reliance materials?

A. Yes.

Q. Okay. Have you read this document, then?

A. Yes, I have.

Q. Okay. I want to ask you about page 4 of

51676 0063

the summary, but certainly refresh yourself, Doctor, if you need to on the rest of the document.

A. Okay. It's been a while since I've read this in extreme detail, but I've scanned it again.

Q. Okay. Well, let me ask my question and if you need to look at it in more detail, please feel free to do so.

A. Sure.

Q. On page, sir, 4 under the summary --

A. Right.

Q. -- there is a discussion of the results that were achieved on this third set of cigarettes when various additives were put in there, as I read the document. And I want to direct your attention to the second paragraph of the results toward the bottom of that paragraph where it says, quote:

Powdered cocoa appears to increase the tumorigenicity of the smoke at both dose levels, unquote.

And it refers above to a lower dose and a higher dose. Do you see where I am, sir, on the left-hand column?

A. Yes, I see.

Q. Okay. First of all, do you understand what the word tumorigenicity means?

51676 0064

A. As used in the NCI study, which is the one we're referring to, tumorigenicity was measured by a biological assay called mouse skin painting. So it was tumor production on mouse skin painting tests.

Q. And do you understand the document to be saying that at the two levels at which cocoa was tested, it appeared to increase the tumor production?

A. That's what this document says.

Q. Okay. Are you familiar with any tests that R. J. Reynolds has done in-house to determine whether the use of cocoa increases the tumorigenicity of the smoke in R. J. Reynolds' cigarettes?

A. I'm aware that our toxicologists have examined this in detail, that they have looked at the bulk of the literature. I think there have been additional experiments conducted after NCI conducted these that were actually in conflict with this conclusion, and cocoa is used as additives and consistent with R. J. Reynolds' policy that additives will not be used if that -- if there is a chance that they will increase the biological end point burden.

So our toxicologists have looked at this very carefully, and their best assessment is that this particular conclusion is in error.

(Mr. Donahue left the deposition.)

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BY MR. WESTBROOK:

Q. All right. And the document itself was issued by the National Cancer Institute, the United States Department of Health, but it was the result, was it not, of a group effort by a number of scientists involved?

A. The National Cancer Institute directed a group called the Tobacco Working Group, which was a long-term -- long-term, multiyear study that was conducted by a group of scientists.

Q. And are you familiar with the members of that group?

A. I'm familiar with some of the members.

Q. Who were the ones that you know?

A. Well, of course, Reynolds had a representative on the Tobacco Working Group. There were -- at two different times. I think the first Reynolds representative was Dr. Murray Sankus; and then after he left, I think that was when he retired from the company, maybe slightly before, Dr. Alan Rodgman took his place on the Tobacco Working Group.

Q. Did Dr. Sankus or Dr. Rodgman issue a public disclaimer or disagreement with this conclusion of the NCI study?

A. I'm not aware of a public -- any kind of

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public document that deals with this issue. I do know that like any scientific research, one comes back and tries to replicate, tries to better understand any conclusions, and I think that's exactly what our toxicologists have done with this issue.

Q. All right. Could you give me a reference, sir, so I could look it up in the medical or scientific literature, of the results of the Reynolds toxicologists' attempt at replicating the cocoa tumorigenicity tests?

A. I don't know whether there are public documents that you can refer to or not. I'm not an expert in this field. I do know that we've looked at this very sincerely and seriously scientifically, and I have confidence that the additives, including cocoa, that we use do not increase the biological burden.

Q. Isn't one of the precepts of good science, Doctor, that you publish your results so that other scientists can look at them, criticize them, comment on them, and advance on them? Isn't that a general precept of scientific research?

A. Absolutely. When that information is not proprietary, I think that's absolutely the approach

that good scientists take.

Q. All right. There would be nothing proprietary about testing cocoa generically to see if it caused tumors, would there be?

A. But, again, I just told you that I don't know whether there is public documents that you can refer to or not. I'm not an expert in this area. I don't keep up with toxicological assessments or biological assessments of the additives. We have experts that do that.

Q. But I'm not asking about public documents; I'm asking about the Reynolds' documents which reflect Reynolds testing cocoa and satisfying Reynolds itself that this conclusion was wrong.

Where are those results published so other scientists could take a look at them the way NCI published its results so Reynolds could look at them?

A. Well, I think I just told you, I'm not sure whether there are published documents or not. I'm not an expert in this area. You'll have to talk to somebody that is.

Q. Okay. But I'm asking you if Reynolds didn't publish its cocoa studies, why not?

MR. McDERMOTT: You're asking the witness

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to speculate. He said he doesn't know whether there have been publications or not. I think the witness has exhausted his knowledge, and you have beaten this horse pretty well to death.

BY MR. WESTBROOK:

Q. Doctor, let me ask it this way and perhaps we can move on. Would you agree with me that if Reynolds has conducted tests attempting to replicate what the NCI did that those tests should have been published in the medical or scientific literature because there is nothing proprietary about testing cocoa?

A. I would have to know more about the situation, and I think that's a decision that an expert in the area should make. I don't know what the bulk of the literature is on cocoa. I do know this: I have read this document. I read its companion documents because they deal with cigarette design.

I don't know the bulk of literature on cocoa and pyrolysis of cocoa. Certainly there is -- I would expect that there is quite a lot of literature out there since cocoa is widely used in many things, not just tobacco, and is heated in many applications. So I don't know.

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Q. Can you tell me another application in which cocoa is smoked other than cigarettes?

A. I'm not aware of another application in which it is smoked, but it's certainly in many foods that are heated.

Q. Doctor, you mentioned a Dr. Alan Rodgman. Is Dr. Rodgman still connected with R. J. Reynolds in any way?

A. Dr. Rodgman retired from Reynolds, gee -- I can't recall the exact date. It's been maybe five, six years ago.

Q. Did you ever speak with Dr. Rodgman about this finding of the NCI that cocoa at two levels increased the tumorigenicity of the smoke?

A. I can't recall ever speaking with Dr. Rodgman about that particular issue. I have spoken with our toxicologists about that particular issue as I went through and read the NCI TWG reports.

Q. Who did you speak with at Reynolds about this issue?

A. It's been a while ago. As I recall, it was Dr. Cooper Rese, one of the toxicologists. I may have spoken also with Dr. Deborah Pence also on this issue.

Q. Is that P-E-N-T-Z?

A. P-E-N-C-E.

Q. Did you work for Dr. Rodgman at R. J. Reynolds?

A. There was a time I reported to Dr. Rodgman.

Q. And what was his position in the company at that time?

A. He was in charge of the research side of Research and Development.

Q. Did you regard Dr. Rodgman as a good scientist?

A. My opinion is that Dr. Rodgman is an excellent scientist.

Q. Someone whose views you would regard as views that should be considered with great care?

A. Dr. Rodgman is an excellent scientist. He is very careful in what he does. He and I have historically gotten into disagreements and arguments over many technical issues, but I think he is a very fair, open-minded scientist who has conducted extremely good research.

Q. Is his background also in chemistry?

A. He is an organic chemist.

Q. And you mentioned Dr. Murray Sankus. Did you work with Dr. Sankus at RJR?

A. Dr. Sankus was at RJR only for a brief time after I started with the company, so I had no direct interactions with him.

Q. Did he retire from the company shortly after you came here?

A. Yes. He retired from the company, and I can't remember exactly when. It may have been within a year or so after I joined RJR.

Q. And what was his position in research when he retired?

A. Oh, I believe he was -- he was head of research.

Q. Did Dr. Rodgman succeed Dr. Sankus?

A. Yes.

Q. Was Dr. Sankus in your view a good scientist?

A. I don't know Dr. Sankus. I've never worked with him on any projects like I have with Dr. Rodgman. I've really not read much technical information that he has ever written, so I really can't answer that.

Q. I notice, Doctor, in some of your testimony in court that you testified about matters occurring at Reynolds before 1977 when you came to the company; is that right?

A. Yes.

Q. How do you get that information?

A. I think the job of any good scientist is to go back and thoroughly understand the literature in their field, to try to learn everything they can about what's happened before. And so it really involves reading as much as we can get our hands on and also talking to the scientists that were involved in that research if they're still around at Reynolds. So ...

Q. Is it fair to say, then, Doctor, that anything that you testify about occurring at Reynolds before 1977 is either the result of having read it in a document or having been told it by someone else?

A. I think it's fair to say that prior to my employment, the matters that I testified on are based on the literature that exists in Reynolds, the literature that exists outside of Reynolds in the public domain that relate to cigarette design, and there is quite a lot of that in the public domain that goes well -- much prior to my employment there, and also my discussions of technical issues with scientists who worked in that time before my employment.

Q. So that what you know about what happened

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at Reynolds before 1977 then comes from either what you've read or what you've been told; is that right?

A. It comes from either what I have been read -- what I've read or through discussions with other scientists that were there at the time.

Q. Okay. And how did you go about trying to locate documents concerning events prior to 1977 in order to prepare yourself to know something about what was going on in the company when you were back in college, I guess, in some respects in high school? How did you do that?

A. I went to the library. I went to the Research and Development library. In fact, that was my first big job once I joined the company was to go to the library, collect a lot of documents on cigarette design and understand as much as I could.

As you can imagine, reading day in and day out gets old very fast, and so pretty quickly I got in the lab and started doing my own experiments and continuing to read all along.

Q. Did you also go into various scientists' files and review their files on memos they had written?

A. I can't recall doing that. I did review a number of memos as well as formal scientific

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reports, published reports and all that that were available from the library. But if you're suggesting that I may have gone into someone's file, opened the drawer cabinet and fished through a particular file, I can't recall ever doing that.

Q. Well, I was really not speaking so much about that as maybe going to stored records to go back and see what were people writing back and forth to each other in the Research Department in 1965 and 1969 as opposed to just reading the reports from the library.

A. Absolutely. A lot of the scientific information is captured in memoranda which are not formal reports. Those are stored in the R&D library and archived.

Q. And how are they stored, sir, by author or by subject or some other way?

A. Both. Both. You can search our R&D library by author or by key word. You can also -- I think you can also put time frames on the search.

One of the more useful ways is to actually sit down and talk with scientists who were involved at the time, and they can also help give direction in finding the relevant information.

Q. Dr. Townsend, if you wanted to publish a

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scientific paper on some research that you had done and you prepared a manuscript of it, are you free within Reynolds to publish it before it's reviewed by someone above you in management, say?

A. Let me tell you what our -- what our approach is to publishing outside the company.

Scientists are first encouraged to publish information that is of scientific value to the scientific community that is not proprietary. If a scientist wants to submit a paper for publication in a peer reviewed journal, they have to, first of all, write that manuscript very carefully, very clearly, and then submit it to at least two peer review scientists, people who also work in our department who know something about the area who are not directly involved in that research who can sit back and objectively critique the scientific value and the scientific quality of that research.

It then goes through a series of management reviews after the peer review process, and the management review would include toxicology review, people who understand toxicology, regulatory issues, scientific affairs from the outside. It includes a review by myself as the group director and also includes a review by attorneys.

DAVID E. TOWNSEND, Ph.D. - EX. BY MR. WESTBROOK

Q. You finally got around to what I was going to ask you about.

Who in the legal field reviews scientific manuscripts, proposed scientific manuscripts at Reynolds, before they get the okay to publish?

A. Usually we have -- we have a small number of lawyers who are attached to the R&D Department, physically reside there, even though they directly report to our Legal Department. And the head of that attached group will review it.

Q. Is the legal group in R&D, is that group also a group of scientists/lawyers, or are they lawyers/lawyers, if that makes a difference?

A. They start out as lawyers/lawyers, and they wind up as scientists/lawyers. No, actually they are very good because they try very hard to learn the scientific issues to try to understand the scientific research we do. And that's probably almost as difficult as it would be for me to learn their lawyer job. So I've got to applaud them. They really do a good job.

Q. But Reynolds has enough scientists, you don't need the lawyers reviewing the manuscripts for scientific issues, do you?

A. The lawyers at Reynolds do not review

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scientific manuscripts for scientific issues, absolutely not.

Q. They review it for legal concerns?

A. They review it for patent concerns, for proprietary issues. They also, because of their in-depth understanding of the external environment, review it for those issues, as well.

Q. By the external --

A. But they in no way influence the scientific content of those papers or the scientific conclusions.

Q. Now, you say the external influences. You include in that the regulatory concerns that Reynolds has with the FDA?

A. You know, I don't understand a lot of that, but I think the lawyers certainly have got to look at it for potential regulatory issues, litigation issues and a variety of things.

Q. For instance, if one of the scientists at Reynolds had a manuscript that he or she was prepared to publish that said that nicotine is a drug, that wouldn't get past legal review, would it?

MR. McDERMOTT: Object. No foundation.

BY MR. WESTBROOK:

Q. You can answer, sir.

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A. You know, I don't know -- you know, I think -- well, my experience with the lawyers in R&D is that -- well, I don't know that that's ever occurred. I've never seen that, so ...

Q. You certainly have never seen a published article from any Reynolds scientist saying that nicotine is a drug, have you?

A. I can't recall seeing that in a published article.

Q. All right. Have you seen many published articles and reports from many other scientists and government bodies saying that nicotine is a drug?

A. From bodies outside Reynolds?

Q. Yes.

A. I think many people have concluded or believe that nicotine is a drug.

Q. All right. Now, I take it, sir, that you have never tried to have an article concerning tobacco safety or health published while you were at Reynolds; is that right?

A. Me personally?

Q. Yes, sir.

A. No.

MR. WESTBROOK: Let's mark as next an October 20, 1978 document from Alan Rodgman to a

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Dr. Laurene marked Secret.

(PLF. EXH. 9, Document from Alan Rodgman to Dr. A. H. Laurene dated 10/20/78 stamped RJR Secret, was marked for identification.)

THE COURT REPORTER: Plaintiffs' 9.

BY MR. WESTBROOK:

Q. Doctor, take a look at that if you would, please, sir.

A. Okay, I've skimmed it very quickly.

Q. All right. The document appears to concern a substance called coumarin; is that right, Doctor?

A. That's the subject of this memo.

Q. And the memo was written while you were at R. J. Reynolds?

A. Oh, I guess I was there about a year at that time.

Q. All right. Was Dr. Rodgman in 1978 then the director of research at R. J. Reynolds?

A. Yes, he was.

Q. All right. Now, the document is stamped RJR Secret. Have you seen that stamp on any other documents within Reynolds?

A. Sure.

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Q. What is the secret category as Reynolds uses it?

A. It's pretty loose, and I don't think we have a rigid protocol for what is secret versus confidential.

Q. That was going to be my next question. I've seen some documents stamped confidential and some documents marked secret.

Is secret in any respect considered to be a higher category of protection within Reynolds than confidential?

A. My opinion is no. I think it just -- it's unclear to me why people choose to stamp something secret versus confidential, because I'm not aware of any serious protocol -- any real protocol differences in the two at this point. Now, at this time, in Reynolds, I don't know whether there was protocol for treatment of document status or not.

Q. All right. Is there any written protocol whatsoever that advises R. J. Reynolds' employees on when a document should be stamped either secret or confidential?

A. That's what I'm saying. I'm not aware of such protocol.

Q. Do you have a secret or confidential

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stamp that you use?

A. I don't have a stamp.

Q. All right. Who stamps these documents secret or confidential?

A. Well, usually the secretary will stamp it. And then in this case, Alan Rodgman initialed it.

Q. Does your secretary have a secret or confidential stamp?

A. I think she has a confidential stamp. I'm not sure if she has a secret stamp.

Q. Okay. Have you given her guidelines on when to stamp a document confidential?

A. No. No. And again, I'm not sure that guidelines exist. I think the fact is that -- and, again, I'm speaking for the situation as it is now. I don't know how it was in 1978. But today, there are many documents that are not even stamped either that are certainly proprietary and confidential.

We try to maintain our records within the R&D Department in a very confidential manner, and I don't think the stamp has any particular significance.

Q. How does a secretary know when to use the stamp or not?

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A. Well, I can -- well, I can tell you that in one project that's going on now, the secretary will routinely stamp secret at the top of the document, and there is no reason in my opinion to do it other than that project historically has had a secret stamp. And if she sees that this document pertains to a certain project, oh, that's got to be secret so let's stamp it.

Again, I don't think there is a specific protocol for classification of documents.

Q. Okay. Are there any other classifications at Reynolds other than secret and confidential that you've even seen stamped on documents?

A. Unstamped?

Q. Is there top secret?

A. No, I've never seen that.

Q. All right. Have you ever seen a document at Reynolds that noted that you should read it and destroy your copy after reading?

A. I don't recall ever seeing that.

Q. Have you ever seen a document at Reynolds that was typed for eyes only?

A. Actually, it's interesting that you bring that up, because I saw that for the very first time

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about a week or so ago.

Q. All right. Was that a stamped or a typed logo?

A. It was a stamp.

Q. Was that the first time you had seen such a stamp at Reynolds?

A. That was the first time I recall seeing that.

Q. Have you learned whether that's a higher degree of protection within Reynolds than secret?

A. At least my experience in the R&D Department is that there is no differentiation, that there is no standard protocol among any of these stamps.

Q. From your experience, Doctor, are the secret and confidential stamps overused by people at Reynolds?

A. All of our documents are to be held as confidential, and so I would say, any of the stamps are, number one, redundant; and number two, I don't think there is any difference in secret or confidential or unstamped.

Q. So, in your view then, any document in your Research Department is a confidential document?

A. That's correct.

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Q. Now, turning to the document itself concerning coumarin, Doctor, do you know, first of all, what coumarin is?

A. Chemically?

Q. Chemically or generically or practically.

A. I know what coumarin is as a chemical.

Q. What is it?

A. I can draw it out for you.

Q. Well, I'm not -- I'm not looking for a scientific formula.

Do you know what the substance is and what it's used for?

A. Coumarin has been used as a tobacco flavor in the past.

Q. Let's look at the very first paragraph where Dr. Rodgman is apparently making a recommendation concerning coumarin use. And he says, quote:

Despite the listing of coumarin as a Category 1 chemical that may be regulated under the OSHA proposed generic carcinogen policy, it is recommended that the use of coumarin at levels less than .06 percent on company products be continued, unquote.

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Did I read that correctly, sir?

A. Yeah, you read that correctly.

Q. All right. Now, the document refers to the OSHA proposed generic carcinogen policy.

What do you understand a carcinogen to be?

A. Again, I'm not an expert in this area, either, but my understanding is that a carcinogen is a compound that may cause excess tumors in a particular biological assay that usually involves pretty high dose level, usually involves some animal, and a particular animal tissue and a very specific protocol.

Q. Okay. I think I saw some testimony by you in the past concerning the fact that you believe that Reynolds had discovered approximately half of the known constituents in cigarette smoke; is that accurate?

A. That's accurate, yes.

Q. Okay. And has Reynolds published information concerning the discovery of some of those constituents?

A. We've published extensively. I think we've -- my opinion is we've led the industry in the identification of the constituents in smoke and

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tobacco.

Q. All right. Could you tell me, Doctor, which carcinogens in cigarette smoke has Reynolds first identified and first published in the peer reviewed scientific literature?

A. The first?

Q. Yes.

A. I don't know the first. I would have to go back and look at my records.

Q. Well, I'm not concerned about the first one that Reynolds has published. I would like to know for any carcinogen in cigarette smoke, for any of them, has Reynolds been the first to publish their discovery in cigarette smoke in the peer reviewed scientific literature?

A. Again, I would have to go back and look at the records because I don't remember that off the top of my head.

Q. What records would you look at?

A. I would go back to the R&D library and look at publications that were issued from RJR.

Q. All right. As you sit here today, Doctor, is it correct that you can't think of any carcinogens in cigarette smoke for which Reynolds has first published their discovery?

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A. What I said is I would have to go back and look at the records.

Q. Okay. Now, with respect to coumarin, sir, Dr. Rodgman recommends that the use of coumarin in R. J. Reynolds' cigarettes be continued; is that right?

A. That's what he says here.

Q. All right. And he talks about a level of .06 percent on company products, and I would like to try to understand what that means.

Is that number, .06 percent, the same as 6/10,000?

A. 6/10,000 what?

Q. Well, is .06 percent the same as 6/10,000, .006 as a fraction -- actually as a decimal?

A. Okay, as the decimal fraction of the total weight? It would be a weight percent or a weight fraction.

Q. All right. 6/10,000; is that right?

A. Okay.

Q. And it's not a mental test if you need a pencil to write it down, Doctor.

A. Okay.

Q. Is 6/10,000 the same as 600 parts per

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million?

A. So would .06 percent be 600 parts per million?

Q. Yes.

A. No. No -- yes, you are correct.

Q. Is your final answer yes?

A. I think it's correct.

Q. All right. Just before the buzzer you got yes, so we will give you that one correct. All right.

Would that be the same as 6,000 parts per billion?

A. Yes.

Q. Would that be the same as 6,000 nanograms per gram?

A. Yes.

Q. Okay. So as I read the memo, Dr. Rodgman is recommending that coumarin continue to be used at a level of 6,000 parts per billion stated another way; is that right?

A. Uh-huh. Uh-huh.

Q. Okay. Now, if you would, take a look at the 1994 additives list that the industry released. I think it's in the pile in front of you. Here is the exhibit copy.

51676 0089

And I would like to know, sir, do you find coumarin listed on the industry additives list? And I think they are alphabetical.

A. I don't see it listed.

Q. Do you know when between 1978 and 1994 R. J. Reynolds dropped coumarin as an additive?

A. I'm not sure I can sit here and give you a specific date, but in a general sense, I would say it was in the early to mid '80s.

Q. And why was it dropped?

A. Well, again, I'm not sure, you know -- what I know is from what I've seen from a number of reports and memos, but my -- my take is that coumarin was dropped because of the tox questions.

Q. The tox questions?

A. The toxicological questions, whether or not coumarin is, in fact, carcinogenic, and the speculation that it was carcinogenic -- that it is carcinogenic was receiving more and more attention in spite of the fact that it wasn't clear to the scientific community that it was carcinogenic. We made a decision just to go ahead and take it out of our products and did that.

So, again, I think there is debate in the scientific community about whether it's a carcinogen

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and if so, even what level of carcinogen it might be. We just decided to remove it.

Q. Did you know, sir, that coumarin had been banned by the FDA as a food additive?

MR. McDERMOTT: Did he personally know?

MR. WESTBROOK: Yes.

THE WITNESS: I didn't know that, but I know that coumarin is still allowed in a number of countries for use as tobacco additives.

BY MR. WESTBROOK:

Q. Is it allowed in the United States?

A. No.

MR. McDERMOTT: Is this a convenient point for a short break?

MR. WESTBROOK: Let's take a break.

THE VIDEOGRAPHER: We're going to go off the videotape record now. This concludes tape 1 of the videotape deposition of David Townsend. The time is now 10:56 AM.

(A recess transpired.)

THE VIDEOGRAPHER: Okay. This is a continuation of the deposition of David Townsend in the case of State of Florida versus the American Tobacco Company, and this is the beginning of tape number 2.

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The date is May 27th, 1997, and the time is 11:09 AM. Counsel -- I'm sorry, it's the 29th.

MR. McDERMOTT: Time flies when you're having fun.

MR. WEBBER: I was hoping the 27th, that I picked up two extra days this week.

BY MR. WESTBROOK:

Q. Doctor, you mentioned that coumarin you believe is used outside the United States on cigarettes.

Could you tell me what countries coumarin is used on cigarettes in these days?

A. I'm not sure I can give you an inclusive list, but I think the UK has maximum permissible levels. France and Switzerland have maximum permissible levels set, and I think Belgium allows its use with no maximum level.

Q. Okay. Does R. J. Reynolds sell cigarettes outside the United States?

A. Yes, we do.

Q. Does Reynolds use coumarin in cigarettes sold outside the United States?

A. We don't use coumarin in any of our products worldwide.

Q. Doctor, you mentioned earlier on that a

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DAVID E. TOWNSEND, Ph.D. - EX. BY MR. WESTBROOK

particularly valuable source of information for you in learning what went on in the company prior to 1977 was talking to individuals; is that accurate?

A. Sure.

Q. And you mentioned talking to Dr. Rodgman and Dr. Sankus, correct?

A. Well, I'm not sure that accurately characterizes what I said. I had a lot of discussions with Dr. Rodgman over many years. Sankus, I really didn't know very well. I never really worked with him on anything. I can't recall any serious conversations I've had with Sankus on scientific issues.

Q. And who else did you talk to to learn what was going on in the company pre '77?

A. Who else? Oh, gee, many people. There were a number of people I worked very closely with in cigarette design, like Dr. Mary Stowe, Dr. John Reynolds, just a variety of people.

Q. Are there any other names that come to your mind?

A. Sure.

Q. Who else?

A. Lawrence Cook. I'm sure if I thought about it, I could think of quite a list.

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Q. All right. What was Lawrence Cook's position in the company?

A. He was in Product Development.

Q. What was his position in Product Development?

A. Well, he was in charge of one section of Product Development.

Q. Would he be called a senior scientist?

A. I don't recall exactly what his title was.

Q. Would he be Dr. Cook?

A. I believe he was Dr. Cook.

Q. All right. And when we refer to these individuals as Dr. Rodgman, Dr. Cook and, of course, I call you respectfully Dr. Townsend, none of the individuals who we've spoken about so far have been medical doctors, are they?

A. No. These are scientists, usually chemists.

Q. Okay. And scientists when they get a Ph.D Degree are then referred to in some circles as doctor, correct?

A. In some circles.

Q. Okay. Within the company, I assume you don't call each other doctor; you probably call each

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other by your first names?

A. That's right.

Q. Okay. And you talked about a Dr. Stowe?

A. (Moves head up and down.)

Q. All right. What was Dr. Stowe's position in the company?

A. She also was a chemist, and she was responsible for some of the basic research in cigarette design.

Q. Did you get any information about what was happening in the company prior to 1977 from an individual named Claude Teague?

A. I can't recall any serious discussions with Dr. Teague.

Q. Dr. Teague was also a Ph.D doctor?

A. Yes.

Q. And what was his position in the company as you understand it?

A. He was a chemist. Again, I never directly worked with Dr. Teague on any projects. My earliest recollection of Dr. Teague is he was director in charge of the physical facilities of our R&D Department. And I think prior to that he was a director in charge of R&D planning.

Q. Director in charge of R&D planning.

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Would that be the person who directs what the Research Department should be looking at over the next couple of years?

A. I think nominally that's correct. I think our R&D planning function, however, is a lot looser than that. Our R&D planning function historically and even today worries a lot about budgets, our facilities, as well as resource and resource allocation.

From time to time, it does make suggestions on R&D strategy. However, the R&D planning function in Reynolds doesn't direct R&D strategy per se. It never has and still doesn't today.

Q. All right. Is Dr. Teague still with the company?

A. No. He retired sometime ago.

Q. About when did he retire?

A. I'll just have to guess. I would say it's in the early '80s.

Q. And do you know approximately how long Dr. Teague had been with Reynolds when he retired in the early '80s?

A. I think he started in the early '50s. I can recall seeing documents that he wrote back in the

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early '50s, yes.

Q. When you came to the company in 1977, then, I assume Dr. Teague was one of the relatively old-timers around in research?

A. That's fair.

Q. And was Dr. Rodgman also an old-timer?

A. That's fair.

Q. Doctor, as a cigarette designer, are you concerned at all about the level of nicotine that's in a cigarette?

A. As a cigarette designer and product development person, of course, we're concerned about nicotine level in cigarettes.

Q. All right. With your 20 years background in cigarette design and your understanding of what is in cigarettes, particularly nicotine, do you believe that nicotine has any physiological effect on the body when it's inhaled in cigarette smoke?

A. I believe it's clear that nicotine does have a physiological effect a lot like caffeine and many other things that are naturally occurring products.

Q. Are you aware, Doctor, whether or not there are specific receptors in the brain that respond to nicotine?

A. I believe that's correct. Again, I'm not an expert in this area, either, but I know there has been considerable research in nicotine receptor -- nicotine receptor research in the brain.

Q. As a 20-year cigarette designer at Reynolds, can you tell me, why does Reynolds want to have nicotine in a cigarette?

A. Nicotine is an important part of tobacco. It's an important part of the cigarette, and it's important in the overall smoking process.

Q. All right. Let's investigate a few of those generalities.

A. Sure.

Q. First of all--

A. Excuse me. Are we through with this?

Q. For now, yes, sir -- tell me what role nicotine plays in the cigarette from whatever aspect you think is most important.

A. Let me give you -- let me give you a practical answer to that, and then we can go from there.

The practical answer is if nicotine is not present in a cigarette or it's extremely low levels, those products aren't acceptable to the consumers.

51676 0098

Q. Okay. So in your view, nicotine has to be in a cigarette at some level in order to sell?

A. There have been attempts to sell cigarettes with very, very low levels of nicotine, and those products are not consumer acceptable and don't sell in the marketplace.

Q. All right. So in your view if the FDA were to come out, first of all -- its regulation of tobacco were affirmed, if the FDA came out and said nicotine needs to be taken out of cigarettes, is it your view that the cigarette industry would dry up in this country?

A. People's acceptance of cigarettes would fall dramatically. I think it would be -- it would have a major effect on the industry.

Q. Okay. Has R. J. Reynolds marketed a cigarette without nicotine?

A. No.

Q. Doctor, are you familiar with testimony that was given by six or seven cigarette executives before Congress a couple of years ago, including one from R. J. Reynolds, concerning, among other things, whether cigarette smoking or nicotine in cigarettes was addictive? Are you familiar with that episode?

A. I'm familiar with that testimony.

51676 0099

Q. Okay. And you're familiar that Reynolds' position was that cigarettes are no more addictive, I think, than Twinkies?

A. Well, I think that's -- that's a strange analogy.

Q. Okay. But that was an analogy Reynolds used, wasn't it, in Congress?

A. Twinkies? I don't recall our CEO using that analogy.

Q. Let me see. I may be wrong.

A. Then again, maybe you're right. I don't know. Maybe you need to check.

MR. WESTBROOK: Let's mark as next the proceedings of the hearings before the Subcommittee on Health and Environment dated March 25th and April 14th, 1994.

(PLF. EXH. 10, Document entitled Regulation of Tobacco Products (Part 1), Hearings before the Subcommittee on Health and the Environment of the Committee on Energy and Commerce, House of Representatives One Hundred Third Congress, was marked for identification.)

BY MR. WESTBROOK:

51676 0100

Q. Doctor, just so you know, what we have marked after the cover page is Reynolds' written submission, and the reference that I was going to direct you to is on page 579, and the statement, quote:

It becomes clear that cigarette smoking is no more addictive than coffee, tea, or Twinkies, unquote, on the right-hand side.

A. 579?

Q. Yes, sir.

A. I see that.

Q. All right. Does that refresh your recollection that R. J. Reynolds told Congress that cigarette smoking was no more addictive than Twinkies?

A. Well, I didn't recall that specifically, the reference to Twinkies.

Q. All right. Well, let's talk a little bit now about smoking. And I want to draw on your experience not only as a cigarette designer, but also as a smoker. And some of this is basic, so please forgive me.

A cigarette pack contains 20 cigarettes; is that right?

A. That's correct.

Q. All right. What would you say a normal puffer -- and maybe use your own experience -- how many puffs would a normal puffer take on a cigarette?

A. I don't think there is a normal puffer. I mean, we can certainly talk about machine smoking. I think smokers smoke with a wide variety of puffing characteristics, so I'm not sure there is a normal puffer.

Q. All right. Would five puffs per cigarette be a conservative estimate of the number of puffs most people take on a cigarette?

A. I think that would be a low estimate based on what we know.

Q. Some people probably puff more than that?

A. That's fair.

Q. Okay. Let's use five to be conservative. A one-pack-a-day smoker then would smoke 20 cigarettes in a day, correct?

A. Okay.

Q. Or 140 cigarettes in a week?

A. Okay.

Q. And then if we take 52 weeks -- and I multiplied this out -- it comes out to 7,280 cigarettes a year. You might want to just take that and confirm it so we have the record straight.

51676 0102

A. I'll take your word for it.

Q. Okay. You might want to use the calculator for the next one, because with the 7,280 cigarettes, if a smoker puffs five times on each cigarette, I have that calculated to be 36,400 puffs per year.

A. Okay, I'll assume that's correct.

Q. All right. And if the smoker smokes for 30 years and puffs five puffs per cigarette, I have that calculated to be 1,092,000 puffs of cigarette smoke over 30 years.

Does that sound about right?

A. I'll accept your calculation.

Q. All right. Would you agree with me, Doctor, that 1,092,000 doses of whatever is in cigarette smoke is a large number of doses?

A. A million and whatever it was?

Q. 92,000.

A. 1,092,000 is a large number.

Q. So whatever the cigarette smoker is taking into his or her lungs, assuming the person inhales, if you are doing it 1,092,000 times, you are giving yourself many, many doses of whatever is in smoke?

A. That's a large number of puffs.

Q. Okay. And certainly 1,092,000 puffs of cigarette smoke cannot be equated with someone eating Twinkies in any respect, can it? Do you know anybody who has eaten 1,092,000 Twinkies?

A. I'm not sure I understand your question.

Q. Well, a person who smokes a pack of cigarettes a day for 30 years inhales 1,092,000 times based on our rather conservative numbers; do you agree with that?

A. I've said I accepted your numbers.

Q. Okay. Do you know anybody who has ever eaten 1,092,000 Twinkies?

A. No, of course not.

MR. McDERMOTT: Object to the form of the question. It's unfair. It's an unfair comparison. A puff, if anything, might equate to a bite, not a whole Twinkie, but this is pretty silly in any event. And I'm not sure how many bites there are in a Twinkie, but we can investigate at lunch.

THE WITNESS: Probably depends on the person.

MR. WESTBROOK: We might do that.

BY MR. WESTBROOK:

Q. Doctor, with 1,092,000 doses of whatever is in cigarette smoke on a one-pack-a-day smoker, do

51676 0104

you agree that it's very important that whatever that person is taking into his or her lungs not contain harmful substances?

A. Cigarette smoke contains a number of constituents, a large number of constituents, at extremely low levels. Whether or not that's harmful is a question I can't answer. I just don't know.

Q. Now, with respect to nicotine, do you view nicotine as a drug?

A. I view nicotine as certainly physiologically active. There is a pharmacology of nicotine, much like caffeine. So I think it depends on how you define a drug.

Q. If you define a drug as a substance that is intended to have an effect on the mind or body, would you assume -- would you define nicotine as a drug?

MR. McDERMOTT: Object to the form of the question. You're asking for a legal conclusion.

BY MR. WESTBROOK:

Q. You may answer, sir.

A. Can you repeat the question?

Q. Yes, sir. If you define nicotine to be a substance that has a physical effect on the mind or body, would you regard nicotine as being a drug?

51676 0105

MR. McDERMOTT: I also object; that misstates the law.

THE WITNESS: It's clear to me that nicotine is physiologically active a lot like caffeine. If nicotine were classified as a drug, then caffeine in the same way would be a drug.

Now, I view nicotine as clearly a constituent of tobacco, a naturally occurring constituent of tobacco that is physiologically active. It certainly is important to the overall smoking process, to the smoking enjoyment, to the acceptance of products.

Whether or not it's legally a drug or not is really outside my area. I can't speak to that.

BY MR. WESTBROOK:

Q. You talked about caffeine, sir.

A. Uh-huh.

Q. Is caffeine in coffee?

A. Certainly.

Q. Are you aware that coffee manufacturers are subject to the Food and Drug Administration's authority?

A. I'm not aware of that.

Q. All right. As food manufacturers, you're not aware that they are subject to the Food and Drug

51676 0106

Administration's authority?

A. I'm sorry?

Q. As food manufacturers, coffee manufacturers, you are not aware that coffee manufacturers are subject to the authority of the Food and Drug Administration?

A. I'm not aware of any of the regulatory details of the various industries. I just really don't know.

Q. Am I correct, sir, that R. J. Reynolds also operates a food division?

A. We have a subsidiary of RJR Nabisco and that subsidiary is Nabisco.

Q. When you said that nicotine has a physiological action, do you mean that it has some physical action on the body?

A. There is physiological action on the body.

Q. Okay. And is that an action on the body that the tobacco companies, including RJR, were aware of, at least have been aware of for the last 20 years?

MR. McDERMOTT: Object. No foundation.

THE WITNESS: You know, I'm not an expert in this area. I think I can only -- I can only

51676 0107

respond in a very simplistic -- and my response as a smoker. It's clear to me that nicotine, like caffeine, has a physical action on the body.

BY MR. WESTBROOK:

Q. All right. How is it clear to you that nicotine has a physical action on the body?

A. As a smoker, nicotine in cigarette smoke has a relaxing effect for me.

Q. How do you know it's the nicotine?

A. I guess for many, many years, I've assumed it was, I suppose.

Q. But you don't know that?

A. Again, I'm not an expert in the area.

Q. But do you know what it is in cigarette smoke that has an effect on you when you smoke?

A. Again, I'm not an expert in the area. As a normal smoker, even prior to my -- for several years prior to my employment at Reynolds, I have assumed probably like everybody else that nicotine has a calming or soothing effect on -- to me.

Q. Now, you say you've assumed it probably like everybody else. Do you believe that all smokers consider nicotine to be an agent that acts on their body when they smoke?

A. I can't speak for all smokers. I don't

51676 0108

know.

Q. Is nicotine addictive?

A. You know, that's, of course, a question that's asked a lot, and it's one that I've thought about a lot. And if by asking me whether it's addictive, if you mean addiction to be that smokers cannot quit smoking, then nicotine is absolutely not addictive. Smokers can quit if they choose to, and they do quit, and they are doing that in record numbers.

Q. All right. Some people quit heroin, don't they?

A. Some people do.

Q. All right. That doesn't mean that heroin is not addictive, does it?

A. I view heroin as an addictive drug.

Q. All right. Despite the fact that people can quit?

A. Some people can quit.

Q. Okay. Have you ever tried to quit smoking?

A. No, I've never tried.

Q. Have you ever been around people who have tried to quit smoking and have had difficulty?

A. Sure.

51676 0109

Q. All right. Have you been around those people and noticed that they have withdrawal symptoms, irritability, things like that?

A. You know, let me give you an example. A couple that I was -- or had been friends with for many years, both the man and woman decided to quit smoking at the same time. One quit very easily. The other was, in fact, very irritable, found it hard to quit, but did quit.

Q. Have either of your daughters tried to quit smoking, sir?

A. Not to my knowledge. I don't know.

Q. Doctor, are you familiar with the statistics showing that among the lung cancer surgery patients who smoke, that after those patients have had a lung or a portion of their lung removed, that almost half of them within a year go back to smoking? Are you familiar with that?

A. I'm not familiar with that statistic.

Q. Would that statistic surprise you in any way?

A. Personally?

Q. Yes, sir.

A. Yeah, I think that would surprise me, sure.

51676 0110

Q. Would that indicate to you that there is something in cigarette smoke that has a significant hold on people that they'll go back to cigarette smoking after they've had a lung removed?

A. I think cigarette smoking is certainly a very strong habit. Your question, is there something in cigarette smoke that causes that -- that habit, you know, I think cigarette smoking includes a variety of things. The taste, the nicotine, certainly, the act of smoking, the ritual of smoking, it's all a package.

Q. You referenced earlier, I think, a decision concerning the FDA and having authority to regulate tobacco. Have you read that decision?

A. No, I haven't.

Q. Is that a decision issued by a judge here in this city?

A. Not in this city.

Q. A judge who sits in Winston-Salem?

A. I think that judge sits in Greensboro.

Q. Okay. Have you discussed the decision with others at R. J. Reynolds?

A. In detail, no.

Q. Do you understand that the Court concluded that nicotine and smoking because of

51676 0111

nicotine could be regulated as drug delivery devices?

A. I understand that in a superficial sense. I'm not a lawyer, of course.

Q. I take it you disagree with the conclusion that nicotine should be regulated by the FDA as a drug or cigarettes as a drug delivery device?

MR. McDERMOTT: Object. No foundation.

THE WITNESS: My personal opinion is that cigarettes should not be regulated as a nicotine delivery device.

BY MR. WESTBROOK:

Q. Suppose Reynolds produced a device which was a long cylinder with white paper on the outside that delivered nicotine, but had no tobacco in it; would you believe that that device would be a drug delivery device or not?

MR. McDERMOTT: Object. No foundation. Calls for a legal conclusion. You may answer.

THE WITNESS: Okay. If it delivers only nicotine?

BY MR. WESTBROOK:

Q. There is no tobacco in it.

A. Then my personal conclusion is, yeah, that probably is a drug delivery device. But

51676 0112

nicotine present as a constituent of tobacco is, in my opinion, not a drug delivery device.

Q. Has R. J. Reynolds developed and marketed any device that looked like a cigarette which delivers nicotine but didn't have tobacco in it?

A. I'm not aware of such a device.

MR. WESTBROOK: Let's mark as next if we could a document entitled Research Planning Memorandum on the Nature of the Tobacco Business and The Crucial Role of Nicotine Therein authored by Claude Teague, April 14, 1972 and stamped confidential.

(PLF. EXH. 11, Document entitled Research Planning Memorandum on the Nature of the Tobacco Business and The Crucial Role of Nicotine Therein, dated 4/14/72, was marked for identification.)

BY MR. WESTBROOK:

Q. Doctor, as a research planning memorandum, would this be one of the documents that would be in RJR's technical library?

A. I believe this document is in RJR's R&D library.

Q. And what I've just handed you, the document, it's not the first time you have seen this

51676 0113

document, is it, sir?

A. I have seen it before. It's been a while since I've looked at it.

Q. Now, in 1972, sir, you were not with the company; is that right?

A. That's right.

Q. This would have been one of those documents that you may have reviewed to try to see what was happening in the company prior to your time arriving there; is that right?

A. Documents going way back, you know, I have reviewed those to get an understanding of what was going on. I can't remember whether I looked at this in my early days of employment or not.

Q. Let's look at what Mr. Teague has to say as of 1972.

MR. McDERMOTT: If you want to examine the witness on this document closely, do you need to take time to look at it, Dave?

THE WITNESS: Yeah, I would like to.

BY MR. WESTBROOK:

Q. Sure. Go ahead, Doctor.

A. It's been a while.

MR. McDERMOTT: Why we don't turn off the camera and take as much time as you need.

THE VIDEOGRAPHER: Okay. Going off the videotape record. The time is 11:37 AM.

(Off-the-record conference.)

THE VIDEOGRAPHER: Back on the videotape record now. The time is 11:42 AM.

BY MR. WESTBROOK:

Q. Doctor, have you had a chance to look at the document that we have in front of you?

A. I've skimmed it quickly.

Q. All right. If you need more times, Doctor, to answer the questions on the document that I ask you, certainly, we will give you that time.

Is it your understanding, Doctor, that as of April 14th, 1972 when Dr. Teague wrote this memo, he was the Director of Research Planning at RJR?

A. I would assume that he were. You know, I don't know that specifically. From this memo, I would assume that.

Q. And, again, this was before your time?

A. That's correct.

Q. Let's look at the cover page of the memo. The title is Research Planning Memorandum on The Nature of the Tobacco Business and The Crucial Role of Nicotine Therein.

I take it from our previous discussion

51676 0115

that you do agree that nicotine plays a crucial role in the tobacco business?

A. Nicotine plays a very important role in the acceptance of cigarettes by smokers.

Q. And this document is stamped confidential.

Would you agree with me, Doctor, that this is a document that R. J. Reynolds would not want out in public either in 1972 or wouldn't necessarily want it out today in 1997?

MR. McDERMOTT: Object to the form of the question. It calls for speculation.

THE WITNESS: Our research library contains a lot of competitive information, not only on scientific research, but on the strategy and alternate approaches to strategy for our research and development.

BY MR. WESTBROOK:

Q. Well, let's look at the first page of the document where Dr. Teague says in the second line, quote:

Tobacco products uniquely contain and deliver nicotine, a potent drug with a variety of physiological effects, unquote.

Is that something that R. J. Reynolds

51676 0116

would want in a public press announcement?

MR. McDERMOTT: Object. No foundation. Calls for speculation.

THE WITNESS: You're asking me really to guess. You know, I'm not sure I understand.

BY MR. WESTBROOK:

Q. Well, you have been a media spokesman for the company, haven't you?

A. I've been a media spokesperson on cigarette fire safety, period.

Q. And you are familiar with the company's policies on what the company will say and not say publicly about its products, aren't you?

A. Let me make it clear. I don't think there is a monolith of what is permissible and what is not permissible to say. We in the Research and Development Department conduct good research, and there is nobody standing over us saying here is what you can say and here is what you can't say.

Q. All right. Well, as the director of Product Development today in 1997, do you have any objection to there being a public announcement made that R. J. Reynolds said that, quote:

Tobacco products uniquely contain and deliver nicotine, a potent drug with a variety of

51676 0117

physiological effects, unquote?

MR. McDERMOTT: I object to the form of the question. It isn't R. J. Reynolds that said this; it's Dr. Teague that said this.

MR. WESTBROOK: Counsel, just as more for identification than anything now, that's about the fifth or sixth time that you've made a speaking objection. That is in violation of the Florida procedures, and I would ask you please to conduct yourself according to those, so we don't have to interrupt this and contact the Court. Thank you.

MR. WEBBER: Was that a ruling, Your Honor, or a statement?

MR. McDERMOTT: You do your job, and I will do mine. My objection stands.

BY MR. WESTBROOK:

Q. Dr. Townsend, back to my question now. With respect to the statement that, quote, tobacco products uniquely contain and deliver nicotine, a potent drug with a variety of physiological effects, unquote, is that a statement you've ever seen R. J. Reynolds make publicly?

A. To your specific question, I've never seen that statement made publicly by R. J. Reynolds.

Q. Let's turn over to the next page, the

51676 0118

beginning of the first full paragraph. Dr. Teague says, quote:

Happily for the tobacco industry, nicotine is both habituating and unique in its variety of physiological actions, hence no other active material or combination of materials provides equivalent, quote, satisfaction, unquote, period.

Do you see that sentence, sir?

A. I see the sentence.

Q. All right. Do you agree that nicotine is both habituating and unique in its variety of physiological actions?

A. I'm not sure what all that means. I do agree that cigarette smoking is a habit.

Q. In your experience 20 years as a cigarette designer at R. J. Reynolds and being around all the other people there designing cigarettes and working on them, has R. J. Reynolds, to your knowledge, come up with any other active material that provides the same physiological activity as nicotine?

MR. McDERMOTT: Can you repeat the question, please? I'm sorry, I think I missed something. Would you mind just reading it back?

(The Court Reporter read the question

51676 0119

commencing on page 118 line 15.)

MR. McDERMOTT: Thank you.

THE WITNESS: In my 20 years of experience at R. J. Reynolds, we have designed cigarettes with tobacco that naturally contains nicotine.

BY MR. WESTBROOK:

Q. Is the answer no?

A. To what question?

Q. To my question.

A. Which is?

Q. The question the reporter just read to you.

A. Can you summarize it again real quickly?

Q. Let's let him read it to you and if can you answer it yes or no, I would appreciate it.

(The Court Reporter read the question commencing on page 118 line 15.)

THE WITNESS: I can't answer that with a yes or no, because in my experience, I'm not aware of research that has been conducted to look at other compounds of physiological activity that may be useful as, if I interpret your question correctly, as an alternate to nicotine.

BY MR. WESTBROOK:

51676 0120

Q. Do you know what a nicotine analog is?

A. I know that there are compounds that are considered nicotine analogs.

Q. And do you know what they are, what a nicotine analog is?

A. A nicotine analog is a compound -- this is my interpretation -- is a compound that carries similar -- certain similar properties of nicotine biologically.

Q. Has R. J. Reynolds to your knowledge worked on nicotine analogs during the 20 years that you have been in research at R. J. Reynolds?

A. R. J. Reynolds has done extensive research looking at some nicotine analogs for the purpose of possible new business in pharmaceutical areas, not as constituents of cigarettes.

Q. Has R. J. Reynolds ever marketed a device that looked like a cigarette which had nicotine removed and a nicotine analog put in?

A. I'm not aware of such a case.

Q. To your knowledge, sir, have concerns about FDA regulation of cigarettes as drugs prevented R. J. Reynolds from replacing the nicotine in a cigarette with a nicotine analog?

A. I'm not aware that any of that research

51676 0121

has been conducted.

Q. As you sit here today, you have not read any such research on replacing nicotine in a cigarette with a nicotine analog at RJR?

A. I'm not aware of that.

Q. Now, you said that R. J. Reynolds had done nicotine analog research as a part of development of new products that are not cigarettes; is that right?

A. I think what I said was as potential new business opportunities in the pharmaceutical industry.

Q. All right. Does R. J. Reynolds have a pharmaceutical branch?

A. No.

Q. Which research and -- research group within R. J. Reynolds did this nicotine analog research?

A. There is a small group of people who have spent time doing it. There has been a variety of different organizational names. I'm not certain what their current organizational name is.

Q. Are they people who work in the tobacco company?

A. Yes.

Q. What is a tobacco company like R. J. Reynolds doing with pharmaceutical research?

A. We have a lot of experience in biology, toxicology, chemistry, a lot of understanding of nicotine pharmacology and kinetics that has come out of our basic research, and there has been research and continues to be research looking at analogs of nicotine that may be attractive to the pharmaceutical industry.

Q. Has this research been done for a pharmaceutical company, or has R. J. Reynolds done the research in-house?

A. We have done the research in-house, and our -- trying to determine whether there is a market in the pharmaceutical industry for our knowledge.

Q. Did you come to Reynolds from a pharmaceutical company or a chemical company?

A. A chemical company.

Q. Did you come to Reynolds as a result of a staff reduction at the chemical company?

A. No, I enjoyed my job very much at the chemical company. I came here because I was getting ready to raise a family, and living in the Northeast was not high on my list of priorities for raising a family. But I had a very good job at the chemical

company, and I enjoyed it very much.

Q. All right. Let's turn over to page 5 of Dr. Teague's document for a second. I want to ask you about a couple of other things. In the first full paragraph toward the middle Dr. Teague states as of 1972, quote:

We have deliberately played down the role of nicotine. Hence the nonsmoker has little or no knowledge of what satisfactions it may offer him and no desire to try it, unquote.

Were you aware, sir, before I read you that statement that as of 1972, RJR was playing down the role of nicotine in cigarettes?

MR. McDERMOTT: Object to the form of the question.

THE WITNESS: I don't agree with that at all. My experience has not been that we have played down the role of nicotine. I think we've made it clear that nicotine is an important part of the smoking process. So I don't agree with this.

BY MR. WESTBROOK:

Q. Do you disagree with it as of 1972?

A. I think I said it's been my experience. If I didn't say it, I certainly intend to say it. But it's been my experience at Reynolds that we, over

the 20 years that I have been here, that we have not played down the role of nicotine, that nicotine is, in fact, important in the smoking process. A primary -- a wonderful example is that one of our competitors, in fact, tried to market a product with extremely low levels of nicotine, relatively high tar levels, extremely low levels of nicotine.

We conducted a lot of research to try to develop similar products. Our competitor test marketed those products, and they weren't acceptable to the consumer. There is no question that it's important.

Q. Let's talk about RJR's efforts now and your experience. Would you tell me since 1977 what efforts R. J. Reynolds has made to highlight to the smoker the effect of nicotine in smoke on the human body?

A. To highlight to the smoker?

MR. McDERMOTT: Object. No foundation.

THE WITNESS: I am not aware of -- I'm not aware of any efforts to highlight to the smoker any research on nicotine effects on the body. Again, I'm a chemist working in product development. I don't know everything that's going on.

BY MR. WESTBROOK:

51676 0125

Q. Let's talk about, and take the word highlight out, what efforts are you aware of in your experience of 20 years at R. J. Reynolds where R. J. Reynolds acknowledged, advertised or spoke about the effects of nicotine on the body in communicating with smokers?

A. R. J. Reynolds has conducted a lot of research, particularly over the last 15 years, on nicotine. We've published most of that work in peer reviewed journals. We've presented it at technical meetings, at scientific meetings, around the world, and the science that we've conducted and the information we've learned is out there.

Now, it's not the kind of information that the public can understand. Frankly, I don't understand it. I'm a chemist, not a biologist.

Q. You anticipated my next question, sir. In communicating with the consuming public, Reynolds has certain ways that it does that, correct?

MR. McDERMOTT: Object to the form of the question. No foundation.

THE WITNESS: Are you talking about smokers or the public?

BY MR. WESTBROOK:

Q. Smokers.

51676 0126

A. We communicate with smokers, in my opinion, through marketing. We also communicate through 800 toll free numbers. There is a variety of ways.

Q. And tell me, sir, specifically in R. J. Reynolds' marketing activities since you have been with the company for 20 years, what efforts has Reynolds made to speak about, discuss or otherwise not downplay the effect of nicotine on the smoker's body?

MR. McDERMOTT: Object. No foundation. Let me point out, this is an area that is covered by preexemption. This man is a scientist and a chemist. This is a bit of a waste of time. I'm not going to stop you from inquiring, but this is pointless.

THE WITNESS: Well, I mean, the actual fact is, you know, I don't know all that marketing conveys to consumers. That's not my area. I work in the laboratory. You know, in a general sense, it's clear to me that as we market cigarettes, there is information provided via toll free numbers. There is information provided to people in the scientific community via scientific presentations, through publications and peer reviewed journals.

51676 0127

There have also been a number or a series -- I can recall a series of -- of informational advertisements where the company will, in fact, publish a half-page or a full-page information article about some aspect of smoking.

I don't know whether this issue was in that or not. I just don't know.

BY MR. WESTBROOK:

Q. Okay. I think we can agree that the vast majority of smokers don't go to scientific meetings on cigarettes, do they?

A. I think that's fair.

Q. Let's look at the last page of Dr. Teague's memo, sir, where he is outlining proposed research activities over the long term. And with respect to number 5, I wanted to ask you about his recommendations that RJR study the means for enhancing nicotine satisfaction via synergists, alteration of pH, or other means to minimize dose level and maximize desired effects.

Do you understand what it means to enhance nicotine satisfaction via synergists?

A. I understand the concept, I think.

Q. Are there certain substances that are believed to act synergistically with nicotine to

increase the effect of a given amount of nicotine as picked up by the body?

A. Again, I'm not an expert in this area, but I seem to recall an account actually in the popular press alleging that there are certain synergists that increase nicotine's effect; and whether that's true or not, I have no idea.

Q. You've seen it in the popular press. Is that in connection with the tobacco litigation that you've read this?

A. As I recall, I think it came out as a result of a document production which then ultimately hit the popular press.

Q. All right. There is a reference, the next reference in Dr. Teague's paragraph, as to the alteration of pH.

What effect does altering pH have on nicotine satisfaction?

A. Well, the whole notion of pH I think is complicated, and I think it's really misunderstood.

Q. All right. Do you understand it as a chemist?

A. I think I do as a chemist.

Q. Let's --

A. The biological questions wrapped around

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it I think are not well understood by me.

Q. All right. Let's back up to a basic question. Is there a neutral dividing line between acids and bases as measured by pH?

A. pH, by definition -- well, pH is the defined logarithmic scale that is a measure of acidity. A neutral solution -- and pH is valid for dilute aqueous solutions only really -- a neutral solution neither acid nor base would be a pH of 7.

Q. Okay. And does nicotine have a natural pH?

A. Nicotine is a basic material in solution.

Q. And does that mean that its pH is above or below 7?

A. It would be above 7 in solution.

Q. Now, how do you measure the pH of smoke in the laboratory?

A. Well, pH can be measured for cigarette smoke -- it's an arbitrary laboratory measure where -- and there are different methods that have been developed to do that. In fact, at Reynolds we've had several methods over the years that have substantial differences.

But, generally, one would take whole smoke into some liquid trap, just bubble whole smoke

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through some liquid, and then after the smoking is complete, you bubble all the smoke through this liquid, and then you take that liquid and place a pH electrode in and read the number.

Q. All right. So, now, do you have a number in mind of the natural pH of smoke? I know you said above 7, but do you have a number in mind?

A. Well, again, this is part of the area of confusion, because pH really is valid for dilute aqueous solutions. Smoke is neither dilute nor aqueous. So while you can measure a number for pH, its strict meaning in the chemical sense in terms of hydrogen ion concentration is questionable.

However, all that said, sure, you can go in the lab and do as we have done, measure smoke pH, whatever that means, who really knows, and you measure a number that's roughly 6, given the protocol that we typically use.

Q. All right. If nobody knows what it means, why do you do it at Reynolds?

A. That's a good question. I think this speculation by Teague of altering pH may enhance nicotine satisfaction -- I think there are a number of other researchers over the years at Reynolds who have speculated about the importance of pH -- has led

to us developing techniques to measure pH, to collecting some data on smoke pH for various products, trying to alter pH and see if that's possible, and to see what the ultimate consequences might be.

And also from a very pragmatic point of view, our product developers have understood over time that through just experience, that if they are developing a new product, if they measure smoke pH, it needs to be within a fairly narrow range to be consumer acceptable. And if pH is on the high side of that range, it's probably not an acceptable product.

If it's on the low side of that range, it's probably not an acceptable product.

Q. Is ammonia one of the substances that Reynolds' scientists have studied to see the effect of that substance on the pH of the smoke?

A. I think ammonia and some ammonia compounds can alter the pH of cigarette smoke if used at high concentrations, high levels. So, yeah, it's entirely possible, but, again, I think in terms of producing acceptable products, what we've found empirically is that if the pH is altered very much toward the high side of this narrow range or toward

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the low side of that narrow range, those products are not acceptable.

Q. What's the range of acceptable pH of cigarette smoke?

A. There is no clearly defined range, and I say that because this is again something that -- product developers -- some product developers approach their tobacco blending expertise, their blending expertise, as an art, and they really do use a wealth of experience and information they've learned in developing products.

So any kind of judgment about consumer acceptability and pH is developer dependent. In other words, some developers don't use pH measurements as any kind of useful measure. Some product developers do use that to judge whether their particular blends, the combinations of Burley, Turkish, flue-cured, Maryland tobaccos and the particular cigarette design gives them a smoke that might be consumer acceptable.

So I can't give you a definite range.

Q. Let's talk about those blenders or scientists who use the pH range. You said there was a fairly narrow range outside which the smoke is not acceptable.

What is the range to which you were referring?

A. That's what I'm saying. I can't be quantitative. I can give you some general ideas. If the smoke pH for cigarettes is typically around 6, if the pH gets above, say, six and a half or 6.8, you are probably getting smoke taste problems. If you get below 6 or 5.8 or something in that neighborhood, then you're probably getting into smoke taste problems.

So, again, the pH range is fairly narrow. But, again, it's not a quantitative measure that is used by scientists at RJR routinely to give them any indication even in a quantitative sense of how that cigarette performs or anything about nicotine satisfaction, for example.

Q. Does Reynolds use ammonia in its cigarette production processes?

A. We use ammonia compounds in some processes. We've in the past used ammonia in the reconstitution of tobacco.

Q. Okay. And what use is ammonia put to in reconstituted tobacco?

A. Ammonia in reconstituted tobacco seemed to improve sheet strength. We currently don't use

that. Ammonia also can react with some compounds in tobacco to form very flavorful compounds, a general class of compounds called pyrazines.

So ammonia and ammonia compounds really do affect the taste, the flavor of the smoke. And used at the levels that we do in our processes, I think you find really not a significant effect on smoke pH.

Q. What effect does ammonia have on the nicotine itself in the smoke?

A. On nicotine itself? I'm not sure I understand your question.

Q. Well, is there something called impact that the folks at RJR refer to in connection with cigarettes, how cigarette smoke feels in the mouth?

A. Sure.

Q. Does ammonia affect at all the impact of cigarette smoke?

A. The addition of ammonia can affect impact. An impact -- impact I'll define as sensory response in the oral cavity, throat and maybe upper respiratory tract. It's simply a sensory response.

Q. Is ammonia --

A. Addition -- excuse me. Just let me make sure I'm clear. Addition of very high levels of

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ammonia and some ammonia compounds can affect sensory impact.

MR. WESTBROOK: Let's mark as next --

MR. McDERMOTT: It's about time for lunch. Are you going to be able to finish up this line?

MR. WESTBROOK: Let's mark as next a document produced by RJR entitled Ammonia.

(PLF. EXH. 12, Document entitled Ammonia, was marked for identification.)

MR. McDERMOTT: Is this the complete document?

MR. WESTBROOK: As far as I understand it. I stand corrected if you've got another page somewhere, but that's as far as I understand.

THE WITNESS: Okay, I've skimmed it.

BY MR. WESTBROOK:

Q. All right. Doctor --

A. Do you know who the author is?

Q. I have the document only as it is. My first question to you was going to be, Doctor, do you know who the author of this document is?

A. I don't know.

Q. Before I handed you this document today, Doctor, had you ever seen it before?

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A. Yeah, I've seen a portion of it. I actually -- I don't recall seeing the last two pages.

Q. So the document that you saw ended on page 4 and didn't have pages 5 and 6 as this document does?

A. As I recall. I could be wrong. That's what I recall.

Q. Okay. All right. Let me direct your attention to page 3, where there is a discussion of some of the historical work on ammonia. In the second full paragraph under the title, it says, quote:

In the early 1970s, a major R&D program was initiated to investigate the physical chemistry of tobacco and tobacco smoke in an attempt to gain a better understanding of the factors affecting smoke harshness, irritation and strength. These studies led to the following observations and conclusions.

And the first one is, quote: The pH of cigarette smoke is important to smoke quality and can be used as a measure of the physiological strength of smoke, unquote.

Is that a conclusion with which you agree, Doctor?

A. I agree with the first part of that

Source: https://www.industrydocuments.ucsf.edu/docs/tggl0001

number one. I don't agree with the second part. I agree that the pH of cigarette smoke is important to smoke quality. As I've said earlier, we've known that empirically. I don't agree that smoke pH can be used as a measure of physiological strength of smoke.

Q. And the second conclusion is that, quote:

Ammonia in smoke is one of the major pH-controlling components, unquote, and it goes on.

Do you agree that ammonia in smoke is one of the major pH-controlling components?

A. I don't really have a basis to make a judgment on that. I think it's reasonable that ammonia can control pH to a degree. Whether it's the major component, I don't know, because there are quite a lot of acids in cigarette smoke which also ought to have a significant effect on controlling the pH, as well as a number of other bases in addition to ammonia.

So it's hard for me in this very complex mixture to pinpoint ammonia and say that is the major controlling component of pH.

Q. Now, according to this document, Doctor, these conclusions are the result of a major research and development program that Reynolds conducted,

correct?

A. That's what it says, yes.

Q. You were not involved obviously in this program based on your answers?

A. No. No.

Q. Turn over to the next page, page 4, sir, and I want to ask you, the first paragraph under the numbered paragraphs where the conclusions are summarized, and then it says that, quote:

Based on the above observations, it was decided to investigate the use of ammoniated reconstituted tobacco (G7A) as a means of increasing the smoke pH of RJRT cigarette products, unquote.

Have you ever heard the term G7A, sir?

A. Sure.

Q. And is that a correct numbering system for ammoniated reconstituted tobacco within RJR?

A. Yes.

Q. Okay. The document continues, quote:

NFO tests indicate that smokers prefer products containing G7A over products containing only G7 (untreated reconstituted tobacco), period. Since the introduction in Camel Filter in 1975, G7A has been tested and/or introduced in 19 additional brands at levels slightly greater than 27 percent, unquote.

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Is that information that G7A has been used in RJR cigarettes at levels of up to -- or levels greater than 27 percent consistent with your understanding of the blends of tobacco components that have gone into Reynolds' cigarettes?

A. I think there have been -- again, depending on the particular cigarette brand style, there have been products that probably get up into the 25-to 27-percent range of reconstituted tobacco. I would say that most cigarettes are probably a bit under that.

Q. All right. Now, this document says that the G7A was used, quote, as a means of increasing the smoke pH, unquote, of Reynolds' cigarettes. Is that consistent with your understanding?

A. Well, I disagree with what you said. It says -- this document says, it was decided to investigate the use, not that it was used, for that purpose.

Q. All right. And after it was investigated, then the G7A reconstituted tobacco was used in Reynolds' cigarettes?

A. G7A was used in commercial products. I think the use of G7A doesn't significantly affect smoke pH. It does affect the taste characteristics.

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We talked about the reaction of ammonia and ammonia compounds with certain tobacco constituents in the production of pyrazines and other flavorful compounds which I think are spoken to if I remember right way back here, and there is a taste difference. No question about it. A pH difference, I don't think that's clear to me at all.

Q. All right. Is it clear to you, sir, that this document says that Reynolds investigated using ammoniated reconstituted tobacco as a means of increasing pH, and then after that investigation was undertaken, the ammoniated reconstituted tobacco was, in fact, used in 19 brands of Reynolds' cigarettes? That's what this document says, isn't it?

A. Yeah. Let me tell you what I think this document says, as well. It says that it was decided to investigate the use of ammoniated G7, reconstituted tobacco, as a means for increasing the smoke pH. I believe that to be true.

But they did investigate G7A as a means of increasing smoke pH. I think there were a number of theories that if one -- that were batted about at the time in Reynolds that if one increased the smoke pH, that would be a direction to go for, quote, nicotine satisfaction or for a variety of other

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reasons. I think there was even one speculation that smoke pH was directly correlated to sales volume, which I think is a real stretch.

At any rate, I believe that that actually happened -- actually occurred. I do believe also that G7A was incorporated in commercial products and in some specific brands up to fairly high levels, in the range, as I said, from 25, even 27 percent is probably reasonable.

However, I don't believe that G7A substantially affects the smoke pH. I believe that G7A is a more flavorful component because -- by virtue of the reactions between ammonia and other ammonia compounds and sugars and other aminoacids to form very flavorful compounds.

Q. But you don't dispute, Doctor, that the addition of ammonia to the cigarette affects the pH?

A. As I said in response to one of your earlier questions quite a while ago, I think if one adds a lot -- a large quantity of ammonia, you can get effects on pH; no question about it. Theoretically, from a chemical perspective, if you add ammonia to this very complex mixture which happens to be highly buffered, sure, you would expect to see some change in pH.

Q. And Reynolds discovered, did it not, that it got increasing physiological satisfaction among smokers as it increased the ammonia content?

A. No, I don't agree with that. I think it's clear to me that what we've seen is increased acceptance and increased taste attributes from the use of ammonia. I don't believe that satisfaction is necessarily the end point.

Q. Didn't Reynolds have smoke panels that tested cigarettes; and as ammonia content was increased, the smoke panels reported increased physiological satisfaction?

A. I don't recall that. I don't recall ever seeing that. I do believe, though, that as G7A was used, those products were preferred by smokers compared to the nonammoniated reconstituted tobacco.

Q. With respect to this physiological satisfaction issue, Doctor, look at the paragraph just above the one we've been reading, paragraph 7 which says, quote:

Smoking panel results show a decrease in smoke irritation and harshness and an increase in physiological satisfaction with increasing ammonia content, unquote.

Isn't that what it says?

A. That's what it says. And this is exactly opposite to, I think, what your question is saying to me. I interpret your question as saying, R. J. Reynolds used ammonia in reconstituted sheet, so-called G7A, to increase pH and get increased satisfaction.

If one increases pH by the addition of a lot of ammonia -- and that's possible to do -- and you make a significant increase, measurable increase in smoke pH, what one sees -- and we know this from empirical experience -- is that those cigarettes are judged as too irritating and too harsh, and it's probably the leading reason why those products are unacceptable.

And this statement is in exact contrast to that.

Q. Well, that was my question, Doctor. Didn't RJR smoking panels show an increase in physiological satisfaction with increasing ammonia content? Isn't that what your own document says?

A. I'm not sure. In this summary, I'm not sure how a smoke panel -- none of the smoke panels that I'm aware of have a measure of physiological satisfaction, so I'm not sure how this was arrived at.

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Q. Well --

A. Excuse me. Smoke panels that I've been familiar with and involved with over 20 years, we measure specific attributes, taste characteristics, physical attributes like the draw characteristics of the cigarette. We measure unlit and lit aroma. We measure puff counts or estimate burning times as perceived by the smoker, you know, a variety of things. But I've never seen a measure of physiological satisfaction.

Q. It's reported in this document that that's what the smoke panel said, isn't it?

A. Well, we would have to go back to the details from that specific experiment, but I'm telling you, I've never seen that in a smoke panel.

Q. My question, sir, simple question: It's reported in this document that as ammonia content was increased, smoking panels reported an increase in physiological satisfaction? That's what the document says, correct?

A. And the document also says in the same sentence that it also showed a decrease in smoke irritation and harshness, and I'm telling you that I think that's in the opposite direction that one would expect. If you were increasing pH by virtue of

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adding ammonia, increasing pH should increase smoke irritation and increase harshness.

Q. But you weren't involved in this major R&D programs that led to these seven conclusions?

A. No. I'm trying to interpret this document just as you are.

Q. Okay. And you will agree with me that after the major R&D program was initiated, these seven conclusions were listed and among them is that as ammonia content was increased, there was an increase reported by the smoking panel of physiological satisfaction? That's what's reported, correct?

A. That's what's said in this document, and I've made it clear that I've never seen a panel have a measure, any kind of measure, of physiological satisfaction. I don't know how that can be done.

Q. Now, smoking panel results and the conduct of smoking panels, that's not your area of expertise at Reynolds, is it?

A. No. Of course not. We have experts that conduct and design smoke panel tests. They also design particular research projects that involve subject smokers, and they actually conduct the results. We as product developers work very closely

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with them, make sure they understand the products that we have, how they are expected to be different. Perhaps use somewhat different protocols for different types of products.

Q. How would you go back and find the raw data on the smoke panel results? You said you would like to see those results. How would you go back and find that?

A. Well, I think there is two attacks. The first is to -- there is three things necessary. The first I think is one really needs to know who wrote this.

Q. How would you find that out within your company?

A. Well, I'm not sure. I mean, I would probably go back since this is probably an excerpt from a larger document, I would go back and take this number in the lower right-hand corner and try to find the document pages that are on either side of that and go from there.

I think it's important to find out who wrote this. I think it's also -- if you wanted to know the answer to that question, which I find intriguing myself, since I've never seen that, that would be the first place.

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The second place is to go to the library and do a search of the data base.

And the third thing is to ask other people who are known to have worked in these areas at around the same time.

Q. Okay. Doctor, since you find it intriguing, I would ask, if you are so inclined, to do so, and then when we next get together, we will take up the issue of who wrote this document and what the actual raw data from the panel said if that's acceptable.

MR. McDERMOTT: We'll take your request under advisement.

(This page contains information to be supplied by counsel and/or the deponent.)

MR. WESTBROOK: It's a good time to break.

THE VIDEOGRAPHER: We are going off the videotape record. This concludes tape number 2. The time is 12:25 PM.

(A luncheon recess transpired.)

THE VIDEOGRAPHER: Okay, this is the continuation of the deposition of David Townsend in the case of The State of Florida versus American Tobacco Company. This is the beginning of tape

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number 3. The date is May 29th, 1997. The time is 1:44 PM. Counsel.

BY MR. WESTBROOK:

Q. Dr. Townsend, as a cigarette designer with 20 years experience, do you believe that nicotine contributes to the taste of tobacco smoke?

A. I believe that nicotine is really important to the overall sensory characteristics of the smoke. I don't believe nicotine per se has a taste, but it certainly is important in the overall sensation of smoking. It elicits a sensory response, particularly in the oral cavity and the throat.

Q. All right. Haven't researchers at R. J. Reynolds identified the taste of nicotine as foul, something like burning rubber?

A. Actually, I've seen that referred to in a document sometime ago and that goes beyond me. I'm not sure I would agree with that.

Q. Have you ever tasted pure nicotine?

A. No, of course not.

Q. Okay. Are you aware that a dose of nicotine about the size of one drop could kill a person?

A. I know pure nicotine, you know, in concentrated form like that can be toxic.

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Q. Doctor, you are aware, are you not, of a product that R. J. Reynolds marketed and sold called Premier, are you not?

A. Yes, I'm familiar with Premier.

Q. All right. And was Premier a cigarette?

A. Yes, it was.

Q. Why was it a cigarette?

A. Under the government's definition, it is tobacco rolled in paper.

Q. Was Premier ever offered to consumers in Florida for commercial sale?

A. No, it was in three test market locations, and unfortunately it failed in those test markets. I would have loved to have been able to offer it to smokers in Florida.

Q. Oh. Nothing prohibited Reynolds from offering it to smokers in Florida, did it?

A. Well, it doesn't make sense if smokers reject the product to go to the expense of marketing a product that's not going to sell.

Q. All right. Who chose the test markets for Premier?

A. Our marketing department.

Q. All right. And they chose not to test market it in Florida?

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A. What I know is that marketing chose three test marketing locations: Two in Arizona and one in St. Louis.

Q. All right. And it was never test marketed, to your knowledge, in Florida, was it?

MR. McDERMOTT: Asked and answered.

THE WITNESS: It was never test marketed in Florida.

BY MR. WESTBROOK:

Q. All right. Now, is there another product that R. J. Reynolds has sold in the recent past called Eclipse?

A. There is a product called Eclipse that's in test market as we speak.

Q. All right. Is that also a cigarette?

A. Yes.

Q. All right. Has that product to date been offered to consumers in Florida?

A. No.

Q. Is there another product that R. J. Reynolds marketed called Winston Select?

A. There is a product called Winston Select. Actually, that's a commercial product that's been on the market for some time. There is also a test market of a different Winston Select in one

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state.

Q. All right. Let's talk about the two Winston Selects so we know about which one we're talking about.

How about the Winston Select that's been on the market for some time; what makes that product Select?

A. Winston Select is a brand style within the Winston family that's actually nationally available. It's a conventional product, nothing unusual in its design or construction compared to other products of similar tar categories.

Q. Okay. So without demeaning it, it's a regular type cigarette?

A. It's a conventional product much in the same way of any other products in that same tar category.

Q. All right. Now, is Reynolds also marketing a product called Winston Select which is a different type of cigarette?

A. We are test marketing a product that has a number of significant design changes and that's being test marketed in Winston Select packaging as the Winston Select brand in that state.

Q. All right. Is the previous product that

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I referred to as Winston Select, does the package say Winston Select, also?

A. Both products that we've been talking about carry the Winston Select brand name.

Q. Do they have the same appearance to look at the package?

A. There are some differences in the test market product. The advertising, the marketing is somewhat different. But the logo, the brand name, the package style is very similar. There are some specific differences in the packaging.

Q. All right. Now, the Winston Select, that is, the product that is not a conventional cigarette, what are the general changes that Reynolds has made in that product?

A. There are two major design changes:

The first is a specially designed filter that contains a carbon element to remove certain vapor phase smoke constituents.

The other major design change is a proprietary blend that reduces the overall level of nitrogenous compounds in cigarette smoke.

Q. By nitrogenous, does that refer to nitrogen-based compounds?

A. Nitrogen-containing compounds.

Q. Is this second Winston Select, which has the special filter and special tobacco, is that currently available to Florida smokers?

A. No, it's available only in Oklahoma as we speak.

Q. Okay. Was one of the purposes of the Winston Select that's in the test market to reduce nitrosamines in smoke?

A. That was one of the expected benefits. That was one of the objectives of that product, to reduce nitrosamines along with a number of other smoke constituents from a variety of classes of compounds within smoke.

Q. And are you familiar with your experience at RJR that nitrosamines have been identified as carcinogens?

A. I'm aware that some nitrosamines have been identified as animal carcinogens at high levels.

Q. All right. And there are some nitrosamines, are there not, that are called tobacco-specific nitrosamines because they only occur in tobacco?

A. There are several tobacco-specific nitrosamines that occur in tobacco only.

Q. All right. To your knowledge, did

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R. J. Reynolds ever identify and publish initially in the peer reviewed literature the discovery of any tobacco-specific or any other nitrosamines?

A. I'm not aware that Reynolds was the first to publish the existence of these tobacco-specific nitrosamines in the peer reviewed literature; however, we have done extensive analysis. We've developed analytical methods for detecting these at even very low levels, and we've conducted extensive research on ways to reduce them.

Q. Do you have a scientist or group of scientists who come to mind when you think about the scientists who have done most of the work in the outside scientific field on nitrosamines?

A. The one scientist that comes immediately to mind when you mention tobacco-specific nitrosamines outside the industry is Dr. Dietrich Hoffmann, who has done quite a lot of work looking at nitrosamine levels in tobacco and tobacco smoke.

He has also speculated on mechanisms of formation of tobacco-specific nitrosamines and also speculated on possible ways to reduce their levels.

Q. All right. Where is Dr. Dietrich Hoffmann employed?

A. He is currently at the American Health

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Foundation.

Q. And where is that?

A. That's in New York. It's actually in Westchester County.

Q. Has R. J. Reynolds to your knowledge provided any financial support for Dr. Hoffmann's work on nitrosamines?

A. No.

Q. Has R. J. Reynolds to your knowledge provided any financial support for any of Dr. Hoffmann's research on tobacco and health?

A. No. I'm not aware of any support for Dr. Hoffmann.

Q. I noticed in some testimony that I read that you referred to Dr. Hoffmann and a Dr. Wynder quite often; is that right?

A. That's correct.

Q. Do you regard Drs. Hoffmann and Wynder as respected researchers in the field of tobacco and health?

A. Dr. Hoffmann and Dr. Wynder both I regard as excellent scientists. They have been in the field and done extensive research in the area of cigarettes, tobacco smoke or cigarette smoke, tobacco constituents for many, many years. They certainly

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are not pro smoking, pro industry. In fact, I would categorize both of them as antiindustry people.

However, that said, they are good scientists.

Q. All right. Can you identify for me any outside researchers who have done significant work on tobacco and health matters who you would identify as pro tobacco?

A. That's a difficult question. I'm not sure -- I'm not sure I could answer -- I mean, I would just be guessing. I'm not aware of any outside researcher that is clearly pro tobacco. I think there are many researchers who try to keep open mind -- an open mind in their research even though they may have specific biases against the industry.

Dr. Hoffmann and Dr. Wynder are two of those.

Q. Now, when you say they have specific biases against the industry, what do you mean they have a bias against the industry?

A. I know Dr. Hoffmann, and we've had many scientific discussions, and it's clear to me that Dr. Hoffmann would like to see people not smoke.

In spite of that, he continues, I think, by and large to do his best and to be a good

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scientist.

Q. All right. Don't you believe that whatever views Dr. Hoffmann has on why people shouldn't smoke are the result of his scientific work?

A. Well, Dr. Hoffmann can draw whatever views he -- he wants to on why people smoke. I can't speculate on why he has come to that conclusion.

Q. All right. But you described his view and Dr. Wynder's view as a bias. Why do you regard it as a bias when they think people shouldn't smoke after they have done the research that they have done? Why is that a bias?

A. Well, I think they have their own personal opinions as most everyone does about whether or not people should be allowed to smoke or people should smoke.

Clearly there are some people who believe that cigarette smoking is -- is legal and is a practice that's open for personal choice. There are other people who believe that people absolutely shouldn't smoke and that cigarette smoking should be banned in this country.

Their personal opinions about that, however, I think are theirs and theirs only based on

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whatever information or decisions that's gotten them to that point, to that decision.

The thing I'm interested in is in spite of that, regardless of which side you're on, whether you are in favor or against smoking, can you still be a good scientist and be objective in the scientific work that you do. That's the important thing.

Q. All right. All right. Let's take them one at a time. Has Dr. Wynder published a lot of articles on smoking and health matters over the years?

A. Dr. Hoffmann has published extensively on smoking and health issues. Again, as we talked about a few minutes ago, I think one of his focuses has been tobacco-specific nitrosamines.

Q. How about Dr. Wynder; has Dr. Wynder published a lot of articles on smoking and health matters?

A. Dr. Wynder published articles, quite a few articles, on smoking and health issues, but I think in recent years, however, he hasn't published as much.

Q. All right. Do the work of Drs. Wynder and Hoffman go back over the decades into the '60s, for instance, on smoking and health?

A. I think their work goes back into the early to mid '50s.

Q. Now, you said, I think, that you know Dr. Hoffmann; is that right?

A. Yes. Dr. Hoffmann and I have had numerous scientific discussions and have been at various meetings.

Q. Did you serve on a panel convened by the National Cancer Institute to look into the FTC method of measuring tar and nicotine in cigarettes?

A. I was at that meeting, and let me make it clear what my role was. The NCI was asked by the Federal Trade Commission to convene this panel of, quote, experts to address several questions.

The panel included, I think, eight or ten members who were asked to come to conclusions on those several specific questions.

The NCI also invited expert participants who were not officially panel members. So I was an invited expert participant and presented information to that panel, also entered or engaged in some discussion and debate of the issues over the course of a couple of days, but in the end was not -- by not being an official panel member was not allowed to participate in drawing conclusions.

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Q. Dr. Townsend, did representatives of the tobacco industry attempt to keep Dr. Hoffmann off that NCI panel?

A. This is -- the short answer is, yes, there was a, I think, in my opinion, an entirely misguided attempt by one individual to try to keep Dr. Hoffmann off that panel.

Q. Dr. Townsend, in the 20 years that you've been designing cigarettes, you're aware, are you not, that the surgeon general has come out with a number of reports concluding that smoking causes various diseases?

A. I'm aware of that.

Q. All right. And there have been other public health bodies and other scientific organizations that have come out with estimates of how many people, how many thousands of people, smoking cigarettes has killed per year; you are familiar with those numbers, are you not?

A. I have seen quite a variety of numbers along those lines.

Q. All right. And the numbers range into the hundreds of thousands of people killed per year by cigarette smoking; you are familiar with that, are you not?

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A. Well, again, I've seen a variety of estimates. I can't recall any specific numbers, but I've seen a variety of estimates.

Q. And if those estimates are accurate or approximately so, is it true that you have been working on the design of a product that has been found to kill thousands of people a year?

A. I think most people, including the surgeon -- the various surgeon generals and probably most smokers in this country, have decided that cigarette smoking causes some diseases, including lung cancer. They've decided that without classical and complete scientific basis.

Cigarette smoking may cause those diseases, but I think scientifically it's not clear that cigarette smoking per se does. I think what is clear is that cigarette smoking is a risk factor for a number of diseases like lung cancer.

Cigarette smokers as a group tend to have higher incidence of lung cancer and certain other diseases, and whether cigarettes themselves per se cause lung cancer is still not scientifically known. It may be the case.

Q. Is it fair to say, Dr. Townsend, that your view is not shared by any public health

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authority in this country?

A. Well, that's quite a broad sweeping statement. I would probably speculate that it's probably not shared by people in the public health community, but whether it's everybody in the public health community, I have no idea.

Q. Can you identify for me any public health official or any public health group or any public health panel that has concluded, as you just said on behalf of R. J. Reynolds, that it's not proven scientifically that cigarette smoking causes disease?

A. Identify a public health official?

Q. Or group or body that says that.

A. No, I really can't. I'm not terribly well plugged into the public health community. In fact, not at all. So, you know, again, to answer the earlier question, I'm not sure where everybody stands on the issue.

Q. Let's talk a little bit about the FTC, the tar and nicotine ratings.

Was the panel whose proceeding you attended but I understand you did not sit on the panel, was that group looking into whether the FTC method accurately measured tar and nicotine consumption by a smoker?

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A. We could go back to the proceedings of that meeting and look specifically at the three -- I think the three major questions that were given to that panel. And so I can just paraphrase, I think, from my recollection.

But the first question was are there -- does -- does the current FTC method need to be altered or modified to better reflect what smokers actually receive when they smoke cigarettes. Now, that's a paraphrase. And, again, I think to be specific, we need to go back to the proceedings.

Q. All right. Do you agree, Doctor, as someone who is knowledgeable in the cigarette design field, that the FTC method of testing tar and nicotine does not reflect what any smoker necessarily is going to receive by way of tar and nicotine from a cigarette?

A. The FTC tar and nicotine measurement does not accurately reflect what any individual smoker receives from a cigarette. There is tremendous variability among smokers in the way they puff cigarettes, the way they smoke cigarettes. There is also a tremendous variability within each smoker in the way they smoke cigarettes from the first puff to the last puff, from cigarette to cigarette, from the

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first part of the day to the last part of the day. The variability among smokers and even within smokers is exceedingly high.

The FTC test method, however, was never intended to represent what any individual or even what the overall group of smokers actually gets. It was intended to represent or to provide comparative information so that smokers can make choices in the marketplace about the relative tar yields of cigarettes so that they could, in fact, make informed choices.

Q. Is it true, Doctor, that because of smoking habits and such things as smoking compensation that a smoker smoking a cigarette with a lower tar and nicotine rating on the FTC rating scale can actually be taking in more tar and nicotine than someone smoking what appears to be a higher tar and nicotine cigarette?

A. I don't believe that. I think based on all the work that we've done and the smoking behavior research that I've seen, as well as replications of human smoking behavior, it's clear to me a number of things:

First, compensation can and does occur. However, compensation doesn't generally occur to a

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complete or 100 percent. That is, if I'm switched to a lower tar product, I may compensate and take bigger puffs or take puffs more often, but I don't do so to the extent that I get the same tar and the same nicotine yield as if I was still smoking the higher tar product. So it can and does occur, but it's not 100 percent complete compensation.

The other thing is even if compensation occurs, the relative yields of tar and nicotine from cigarettes stay pretty much the same; that is, the entire spectrum of choices shift up or down depending on whatever laboratory measure or whatever puffing conditions you take.

And so the relative ranking is maintained regardless of puffing conditions. So to put that into practical terms, let's say the unlikely circumstance that I'm able to smoke a cigarette in exactly the same way from puff to puff, that doesn't happen, but let's assume I can, and we can measure that puffing behavior, we can estimate what I receive under that puffing behavior with that particular product.

Now, if I'm switched to a lower tar product and puffing exactly the same way, I'll get more than the FTC rating would predict, but it's

still substantially lower than the higher tar product.

Q. All right. But that assumes that you're puffing the same way, doesn't it?

A. Yes.

Q. But if part of compensation is that you puff more frequently or inhale more deeply, then your statement won't be accurate, will it?

A. That's absolutely correct. And if you even compensate 50 percent, you're still getting less than at the higher, in general.

Q. All right. Can you tell me, Doctor, if you have in mind any report in the peer reviewed scientific or medical literature that R. J. Reynolds has published on this issue of compensation showing what you say the study shows?

A. Let me refer to three. And I'm not an expert in human smoking behavior or in compensation, but obviously I've done a fair amount of reading in it because it's important to cigarette design.

The first article actually surveyed the body of literature on smoking behavior and compensation --

Q. Okay.

A. -- accumulated all the published

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information from a variety of sources and found that there were probably, as I recall, roughly eight different experiments trying to estimate compensation. The RJR author summarized that information, tried to accumulate the body of information into an overall summary, and the overall summary was exactly as I said: Compensation can and does occur, and it's far from complete.

Q. Let me just stop you a second. Was that RJR original research, or was it RJR review of someone else's research?

A. It was two of our scientists reviewing the public literature, reviewing the scientific literature, and accumulating all that into one overall critical review of the scientific information.

Q. Are you familiar --

A. So that particular -- to be specific, that particular publication was not new RJR research.

Q. Okay. So let's put that one aside. What I want to focus on is new RJR research.

A. Well, I don't want to put it aside because --

Q. I just did.

A. But I don't want to.

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MR. McDERMOTT: Well, let him complete his answer. He said there were three articles he wanted to refer to. That's the first one.

THE WITNESS: I don't want to put the first one aside because it is the first time that somebody has taken the time to sit down and critically review the information that's in the literature. That process is important for the scientific -- for science to move forward. And it's not a trivial matter to do, so I don't want to put it aside.

BY MR. WESTBROOK:

Q. Okay. Let's go to your second one, and we'll come back to that one.

A. All right. The second publication is -- that I'm familiar with is an experiment to try to estimate intake with normal smokers by measuring cotinine and other nicotine metabolites in urine for smokers who smoke their normal products, their usual brands across the tar range.

In other words, we have a group of smokers smoking higher tar products, a group of smokers smoking lights, a group of smokers smoking ultra lights, and these are all their usual brands, and then finally a group of smokers smoking the lower

products, the one milligram, two milligram products.

Those are their normal products, and then they follow a particular protocol, collect urine, and we measure an extensive battery of nicotine metabolites in their urine to try to estimate intake.

Q. Okay. And who at RJR did that work?

A. Dr. Gary Byrd is the primary author on that.

Q. All right. And was Dr. Byrd's article reviewed in the various layers of review including by the lawyers before it was submitted for publication?

A. Yes, it was.

Q. And was the conclusion of the article consistent with your view, that is, that compensation occurs, but it doesn't occur sufficiently to skew the relative rankings of the cigarettes?

A. The results of that first study surprised me.

Q. And what were the results?

A. The results showed a very strong correlation with FTC yields. So if one plots the FTC tar number with expected tar intake based on the metabolite analyses, there was not only a very strong correlation, but almost a perfect correlation with the FTC yields.

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I found that surprising because we know that smokers compensate, and Dr. Byrd's results suggest that there is very little, if any, compensation going on, because the correlation was too good, actually. Now, that study was a limited study with, I believe, 33 smokers. I was surprised at the results. I think a number of scientists at Reynolds were surprised, and so then that leads us to the third publication.

Q. Okay. Let me just stop you for a second. Am I correct to summarize it, Dr. Byrd's first study concluded that there was no compensation, contrary to what you and others had expected and read from previous studies?

A. I think at best, Byrd's study would show that there is marginal or minimal compensation. I, based on our own internal human smoking behavior research, as well as that conducted by some of our competitors that they've published, as well as that conducted by people outside the industry, all of that body of information together was inconsistent with Dr. Byrd's initial data.

Obviously, with 33 subjects, that's not a big data set. This is a very difficult experiment to do, as well, to try to ensure compliance to such a

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tedious and invasive protocol, a protocol that really overtakes a person's normal daily behaviors. So obviously then that led us to do another experiment.

Q. All right. And what was the next experiment?

A. The next experiment included a refinement to the protocol of the 33-smoker study and increased the sample size to 100 smokers and tried to get better representation across all four tar level categories. Very difficult to find smokers in the one-to two-milligram category. There are not many of those smokers around.

But we tried to get a more balanced representation for the purposes of this experiment.

Q. Okay. And what was -- was that also under Dr. Byrd's auspices?

A. Yes.

Q. And what was the conclusion when he went at it a second time?

A. With the 100 smokers and with the hopefully refined protocol, Dr. Byrd found statistically significant differences in intake across the FTC tar range; however, the differences were not large. And so if anything, his 100-smoker study is on the far side of the bulk of the

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literature, as we talked about a minute ago, from his 33-smoker study.

So now we have the bulk of the literature that's pretty much in the middle between no compensation and full compensation. We have Byrd's first study that came out closer to no compensation. We have his second study that came out closer to full compensation, although there were still statistically significant differences in both cases.

What's the truth? I'm not sure. I still stand by what I said a few minutes ago, and that is, compensation can and does occur. I don't know to what degree it occurs. I think these are very difficult experiments to conduct. I think the one thing that Dr. Byrd has made an advance in is developing analytical methodology for quantitating a more extensive list of nicotine metabolites in urine. That clearly is a scientific advance which didn't exist before.

And the answers from this -- from all three of these pieces I think tell me this is a very difficult experiment -- a very difficult experiment to conduct. The answers probably depend on how you conduct that experiment, the protocols, how many smokers, the distribution of those smokers. And I

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think more work is needed, frankly.

Q. All right. Is it accurate to say that the results of Dr. Byrd's two studies are inconsistent with each other?

A. That's fair to say. I think, again, there are differences in the protocol, in the number of subjects. The two answers from the two Byrd studies are different. They fall on either side of the bulk of the scientific literature today.

And, again, I don't know what the answer is other than this is a very difficult experiment to do. It probably depends -- the answer depends on how you do the experiment and I think, as I said before, more work is needed.

Q. Has R. J. Reynolds done other smoker compensation studies that have not been published?

A. Well, sure. We've done smoking dynamics or puffing behavior studies that haven't been published, where we actually measure puff volumes, puff frequencies for actual human subjects.

Q. Now, those studies are not proprietary in any way, are they?

A. Well, actually, there is some proprietary, I think, nature about some of it. Some of it is probably not proprietary, but I think -- I

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think a portion of it is, yes.

Q. All right. Scientists sometimes when they deal with a proprietary product or a brand name will publish an article without specifically identifying the product tested by name, correct?

A. Right.

Q. Is there any reason why R. J. Reynolds hasn't published its puffing studies with the proprietary information redacted?

A. I think some of the information that we have on puffing dynamics could be published. There is no question about it. I don't think it's terribly different from what's already in the literature. I do think that a portion of what we have seen is proprietary because it deals with cigarette design and how it -- how certain -- particularly physical aspects of cigarettes, like pressure drop, may affect draw characteristics.

Q. Doctor, where are Dr. Byrd's two studies published?

A. The first one is published -- the second one actually is in press right now as we speak. I think he is planning to present it at a scientific conference in the next month or two.

The first one, I can't remember the title

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of the journal. It's the Journal of Psychopharmacology, I believe, but I'm not absolutely certain of that.

Q. Doctor, in the 20 years that you have been designing cigarettes for R. J. Reynolds, is it true that the tar and nicotine levels of your leading brand, Winston, have not changed significantly?

A. The full flavor style of the parent Winston brand -- I'm sorry, let me start over.

The full flavor or the higher tar Winston product from the Winston brand family has really not changed significantly. I would say -- and I'm going way back in my head, and so this is just a guess at this point -- I would say the differences are between -- over that time period range from 17 to 18 milligrams per cigarette down to maybe 15 or 14 milligrams per cigarette.

So there has only been a several milligram swing over the years.

Q. All right.

A. The difference that has occurred is that the market has shifted to lower tar products, and the lights category, those products under 15 and the leading products in the lights category are about 10 milligrams per cigarette, those products have become

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the biggest sellers in the U. S. The lights category is now the biggest segment of the market.

Q. And as you recall, Doctor, Winston at one time was down to the 14, 15 tar range?

A. I think there was a time when Winston was down around 15, maybe as low as 14.

Q. All right. And is it now back up around the 18 range?

A. No, I think it's 16, 17.

Q. Let's mark as next the Federal Trade Commission 1995 report on tar, nicotine and carbon monoxide of the smoke of 1107 cigarettes.

A. The smoke of what?

Q. 1107 varieties of domestic cigarettes.

(PLF. EXH. 13, Federal Trade Commission report entitled Tar, Nicotine, and Carbon Monoxide of the Smoke of 1107 Varieties of Domestic Cigarettes dated 1995, was marked for identification.)

BY MR. WESTBROOK:

Q. Doctor, for the record, I've copied the pages that deal with Winston and Salem.

A. Okay.

Q. If you would, Doctor, take a look at it, and if you would direct your attention first to the

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Winston values.

A. Okay.

Q. I wanted to ask you, first of all, what does king size mean in terms of length for a Winston?

A. That's generally an 85-or an 84-millimeter product in length.

Q. Okay. All right. So with respect to the Winston king size as recorded by the Federal Trade -- reported to the Federal Trade Commission in 1995, what was the tar rating for Winston?

A. Well, Winston King Filter SP, which stands for soft pack, is the leading Winston brand style.

Q. Okay. What is that?

A. The tar is at 17, nicotine 1.4 and CO at 14 all in milligrams per cigarette.

Q. What is the Winston King Hard Pack?

A. The Winston King Size Filter Hard Pack is at 18 milligrams, 1.3 nicotine, and 17 carbon monoxide. The Winston King Filter Hard Pack is actually a pretty small seller.

Q. Okay. So we have the soft pack at 17 milligrams of tar and the hard pack at 18 milligrams of tar; is that right?

A. Right.

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Q. All right. Are there actually different cigarettes that go in the hard pack and soft pack?

A. Not substantially, no. One of the things -- one of the things that is different between a soft pack and a hard pack is that the length dimension is a millimeter or two different. And so generally, the design is slightly different, a slightly different filter, but -- but the differences are minimal.

Q. All right. Now, the Winstons that you said went down to 14 or 15 at one time, were those the Winston King either hard pack or soft pack?

A. Soft pack.

Q. Soft pack. And now the soft pack is back up to 17?

A. Right.

Q. Did you design it to go back up to 17 in recent years?

A. No, there hasn't been an intentional design to bring it up, as I recall. I think there were -- there was a time when -- the cutoff for a lights product is generally accepted to be about 15 milligrams. We already have a Winston Lights product that is right around 10 milligrams, and we didn't want the full flavored version to become classified

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as lights.

We want to give smokers the range of products in each category, so we need to make sure that the full flavor is, in fact, full flavor and is above 15. So that's -- but, you know, again, I'm not aware of an intentional change to increase tar for any purpose at all.

Q. Well, Winston King was at 14 or 15, and now it's at 17 or 18. What did Reynolds do to increase the tar 20 percent?

A. We're always making changes to the products, paper changes, filter changes, going to different filter suppliers. Because tobacco is an agricultural product and is hardly ever the same from year to year, we're making some small blend changes all the time to -- to keep up with this variable agricultural crop.

So I think there has been -- there is always a number of changes to Winston. It's entirely possible to go back and look at specific design specifications for each product back through time. We can go back and look specifically at all the changes that have occurred over whatever time period you're interested in.

Q. But R. J. Reynolds intentionally raised

the tar in Winston to bring it above 15 after it dropped below 15, didn't it?

A. Well, I think what I said was that we didn't want full flavor product to drop into the -- into the lights category. And so keeping it above 15 is important. We have to report these numbers to the FTC. Any claims about full flavor, lights or ultra lights have to be consistent with -- excuse me, with these categories -- with these ratings categories, and, you know, there are always small changes going on.

Q. Is a 20-percent change in tar level considered to be a small change at Reynolds?

A. Products will vary from year to year by a milligram or two very easily without just a whole lot of design change. That's the nature of the -- the nature of the product. What we've got to do is make sure that we are accurately advertising the correct levels under the FTC protocol and that's what we did.

Q. And your business has been cigarette design for 20 years. Does that include the blend of the tobaccos that goes into cigarettes?

A. Yeah. Most of my personal attention has been on physical characteristics of cigarettes, cigarette paper, filtration, filters, air dilution,

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you know, those types of design parameters. Tobacco blending is not one of my main strengths. I have learned some, particularly over the last five or six years, about tobacco blending, but I'm certainly not an expert in tobacco blending.

Q. Did you learn about tobacco blending in preparation for your appearances in court in cases involving Reynolds?

A. No, I don't think that's fair at all. I've learned most of what I know about tobacco blending because it's my responsibility to get new products on the market.

Q. All right. From what you know about tobacco blending then, how does Reynolds raise the tar of Winston 20 percent over the course of a couple of years?

A. By 20 percent, you know, I don't want this mischaracterized because by 20 percent, we are still talking about only a couple of milligrams, two or three milligrams. That's not a lot when you are dealing with a variable product like tobacco.

There are changes in the tobacco raw materials. There are changes in papers and filters that occur naturally. For example, years ago, a number of years ago, we went from flax cigarette

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papers to wood pulp cigarette papers, a change that does make a slight difference in the overall puff count and consequently in the overall yields.

So this is an extremely variable group of materials that we're putting together into a product and trying to ensure that we're reporting to the FTC plus or minus about a half a milligram. But it varies.

Q. Does Reynolds report on Winston packs the tar and nicotine figures for the blend that's going out in the pack?

A. You mean for the cigarette that's going out in the pack?

Q. Yes.

A. Reynolds reports as required by FTC tar and nicotine numbers in advertising, not on the packs.

Q. Let's talk about Salem. Over the years 1977 when you came with Reynolds until the present, have the Salem tar and nicotine figures changed much?

A. Well, you'll have to tell me specifically what brand style you are talking about.

Q. Let's look at Salem King Soft Pack because we talked about Winston King soft pack.

A. Right. I don't think there has been much

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of a change at all in Salem King Size Soft Pack.

Q. By the way, where is the Salem that you smoke on this chart, Doctor?

A. I smoke Salem King -- where is it? I smoke Salem King Filters Soft Pack Ultra Light. Do you see that? It's right before Salem Gold. Salem King Size Filter Soft Pack Ultra Light.

Q. Okay. So you smoke a five milligram tar .4 milligram nicotine cigarette?

A. That's correct.

Q. Is there a tar-to-nicotine ratio that Reynolds tries to keep its cigarettes observing?

A. No.

Q. Does nicotine fluctuate independently of tar in cigarettes?

A. No.

Q. Does nicotine follow reductions in tar on a linear basis?

A. As we make changes to the cigarette design to reduce tar, nicotine pretty much proportionately is reduced in the same way. It's not exactly, so it's not exactly the same ratio, because many of the tools that we use like filtration and air dilution, particularly, have slightly different efficiencies for tar and nicotine removal.

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So the ratio is pretty much the same, and if one looks historically at the tar reductions, the nicotine reductions pretty much follow the same trend. It's just not exactly the same because the design tools have slightly different effects on tar versus nicotine.

MR. McDERMOTT: Time for a break?

(Off-the-record conference.)

THE COURT REPORTER: We will now go off the record. The time is approximately 3:32 [sic].

(A recess transpired, and Mr. Weber left the deposition.)

THE VIDEOGRAPHER: Okay, previously off the record at 2:32. We are now back on the videotape record at 2:42. Counsel.

MR. WESTBROOK: Just so that the record is clear, the reporter announced we were off the record, I think, at 3:32 and actually it was 2:32 and everybody agrees that that is the proper correction.

BY MR. WESTBROOK:

Q. Doctor, let me ask you about Dr. Wynder and R. J. Reynolds' support or nonsupport of his work. Has R. J. Reynolds to your knowledge ever supported the research work of Dr. Wynder on smoking and health?

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A. I'm not aware of such support.

Q. All right. You mentioned that Drs. Wynder and Hoffmann are connected with a group called the American Health Foundation; is that right?

A. That's correct.

Q. To your knowledge, is that a nonprofit organization?

A. I don't know whether it's a nonprofit organization or not. I do know that they accept contract research.

Q. How large, Doctor, is your Research Department at Reynolds?

A. Presently, there is about 450 employees in R&D. That's a ballpark number.

Q. And how large a research budget do you have?

A. Our total R&D budget presently is about 62 or 63 million.

Q. Do you play a role in preparing the research budget for your division each year?

A. I'm responsible for the budget for my research group every year.

Q. Doctor, are you aware that in 1990, R. J. Reynolds told an elementary school principal, I believe, that the tobacco industry had spent $162

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million over the years to support research on tobacco?

A. I don't recall that number.

MR. WESTBROOK: Let's mark as next a January 11th, 1990 document on the letterhead of R. J. Reynolds from the manager of public information at R. J. Reynolds, Mrs. Jo Spach, S-P-A-C-H, to the principal of the Willow Ridge School.

MR. McDERMOTT: I would note for the record that is -- the Willow Ridge School is in Amherst, New York, not Florida, and I question its relevance; but if you wish to employ your time in this way, you may.

(PLF. EXH. 14, Letter from Mrs. Jo F. Spach, Manager, Public Information, Public Relations Department, to Principal, Willow Ridge School, dated 1/11/92, was marked for identification.)

THE WITNESS: Okay, I've scanned it.

BY MR. WESTBROOK:

Q. All right. First of all, Doctor, do you know who Mrs. Jo Spach is at Reynolds?

A. I've heard the name, but I don't know her.

Q. All right. When you heard the name, did

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you connect her with public information or public relations?

A. No.

Q. Did you connect her at all with Reynolds?

A. No, I really didn't, but I think I've heard the name.

Q. All right. Now, you have no reason to doubt that this document was written by Reynolds to a principal at a school in Amherst, New York, do you?

A. I have no reason to doubt that.

Q. All right. I would like to direct you first to the bottom of the first page where after describing Reynolds' research efforts and support for research, the Reynolds spokesman says, quote:

Despite all the research going on, the simple and unfortunate fact is that scientists do not know the cause or causes of the chronic diseases reported to be associated with smoking, unquote.

Do you see that sentence, sir?

A. I see that sentence.

Q. All right. What scientists is she referring to, all scientists?

MR. McDERMOTT: I object to the form of the question. No foundation.

BY MR. WESTBROOK:

Q. You may answer.

A. Well, I don't know. I mean, I'm not an expert in this area. My superficial understanding is that science, toxicology and biology, do not understand mechanisms for chronic diseases such as cancer. I think they are getting closer. As they get into genetics, genetic susceptibility, a variety of issues, science is moving forward.

But my understanding is that science doesn't understand the mechanisms of cancer. Now, I don't know exactly what Ms. Spach was referring to.

Q. All right. Certainly there are many scientists in this country who believe they know the cause or causes of the chronic diseases reported to be associated with smoking, aren't there?

A. Well --

MR. McDERMOTT: Objection. No foundation. You may answer.

THE WITNESS: As I testified to one of your earlier questions, I think it's clear to me that many people in this country, probably most people in this country, have concluded that cigarette smoking causes cancer in spite of the fact that the scientific basis for that conclusion is still lacking.

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BY MR. WESTBROOK:

Q. Most scientists in this country who have studied the issue have concluded that cigarette smoking causes cancer; isn't that true?

A. My answer includes probably most scientists. However, most scientists are not experts in the area of causation.

Q. But the Reynolds representative told this school principal in 1990 that scientists do not know the cause or causes of the chronic diseases. Don't you regard that to be somewhat misleading when there are so many scientists in this country who say they do know the cause?

MR. McDERMOTT: Object to the form of the question. The document speaks for itself, and this witness has nothing to do with this document.

THE WITNESS: Again, I think -- I want to make it clear that I'm not an expert in this area. I view this as somewhat of a semantics problem between your answer -- between your question and my answer.

The fact that a large number of people in this country, which probably includes many scientists, have concluded without scientific basis that cigarette smoking causes cancer is their conclusion. The fact is, in my opinion, is that

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science itself, the science of biology and toxicology, has not unraveled the mechanisms of cancer causation.

I think they are getting close to it in the work -- and they are headed in the right directions in the genetics work, the genetic susceptibility, but science has not unraveled the causes.

BY MR. WESTBROOK:

Q. Is it your testimony, sir, that scientists have concluded that smoking causes cancer without scientific basis?

A. I think many scientists have concluded that. Probably the majority of people in this country have concluded that. The surgeon generals have concluded that without scientific mechanisms and details of the causation, without really understanding what it is that causes cancer.

As I said, I think they are getting closer today. Science is moving closer to the answers.

Q. On a scale of one to ten, with ten being conclusively proven, where do you think we are along the scale of proving that smoking causes lung cancer?

A. Again, this is not my area of expertise.

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DAVID E. TOWNSEND, Ph.D. - EX. BY MR. WESTBROOK

I'll try to tell you exactly what I believe about this.

It's clear to me from epidemiology that cigarette smoking is related to a number of diseases. For example, lung cancer. What is not clear is that there is scientific proof that cigarette smoking in itself causes those diseases. There are a number of associated risk factors along with cigarette smoking.

Cigarette smokers as a group do tend to have a higher incidence of certain diseases. No question about it. And cigarette smoking may cause cancer, but the scientific evidence is not complete.

Q. All right. Well, how far along the scale from one to ten does the epidemiology get us in your view to prove that smoking causes cancer?

A. I'm not an epidemiologist. I can give you my layman's view of what epidemiology is.

Q. Well, I wasn't asking you for that, sir. I was asking you -- you talked about there being epidemiological evidence that smoking is associated with cancer.

On a scale of one to ten, with ten being conclusively proven, how far along does the epidemiology move us?

A. That's what I'm trying to answer.

Q. Go ahead, sir.

A. Epidemiology in my opinion -- and again this is a layman's opinion -- is a screening tool for chronic diseases, is nothing more or better than a screening tool to unravel possible causes. Once those possible causes or risk factors are identified, then detailed mechanistic research is needed to demonstrate that those risk factors, in fact, cause those diseases.

So epidemiology is a very important area of science that does identify risk factors that may potentially be causes. Epidemiology can identify acute causes, perhaps, for acute diseases; but when it gets to chronic diseases, I think it's clear that there are -- that it's really -- provides direction for science in unraveling causation.

Now, again, with all that said and done, you know, understand that epidemiology, causation, medical research is not my area.

Q. All right. Let me see if I can get an impression from you at least as to where we are on proving that smoking causes cancer. Are we down toward zero or one, we really don't know, or are we getting close to ten, it's been proven, in your view

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after all these years of research? Where do we sit here in 1997?

A. I don't know that I can put it on a scale. As I said, I think science is getting very close to understanding some chronic diseases like cancer. The genetic involvement, the genetic basis for certain diseases, genetic changes, genetic susceptibility, that science is moving in rapid fashion.

We may be close to determining what causes cancer and whether cigarettes are, in fact, a cause. But I don't know that I can sit here today and say it's on the scale at this point.

Q. Okay. Let's assume that tomorrow an article comes out in the New England Journal of Medicine that's irrefutable in your view that cigarette smoking causes cancer. Would you continue to work at a cigarette company designing cigarettes?

A. If there is clear proof that cigarette smoking causes cancer and how that happens is known as a result of that research, then what that would do is point me and other researchers in Reynolds and in the rest of the industry clearly in directions that can fix the problem.

I've spent most of my professional life

at Reynolds understanding cigarette performance and cigarette design in an attempt to substantially reduce chemistry and biology in an effort to reduce the potential risks of cigarettes. If we know that cigarette smoking, in fact, causes cancer, the mechanism is known, and we know how it does that, then we know what to fix.

One of the problems we've had, one of the problems I've had and my company has had is trying to hit a moving target of suspicions of what may be why cigarette smoking is a risk.

Q. Okay. Let's talk about that a second. You say your company has been trying to hit a moving target, and I've seen some testimony where you've talked about you read or your company reads in the literature that there is a substance in cigarettes which is thought to be carcinogenic, and you work on that substance, and then you move on to another substance.

Is it your testimony, sir, that scientists have identified various carcinogens or suspected carcinogens in cigarette smoke and then Reynolds works on it and then the scientists say, well, that's not the problem?

A. I see how you can get that from the

testimony. I think that's an oversimplification. Because if you look at the various constituents that have been thought to be a problem -- for example, the list of constituents that are on the surgeon general's list of problem compounds in smoke, or the list of IARC, the International Agency for Research Cancer, if you look at those extensive lists, we have addressed each one of the allegations about the specific constituents, and we've gone in and tried to identify whether or not those constituents are present in smoke.

We've tried to quantitate their levels, and we've tried to reduce or eliminate those compounds. No question about it. But if the scientific community then moves on and says, wait a minute, there is not enough benzo[a]pyrene, for example, to account for the mouse skin painting results, and we don't think that is the problem, Reynolds hasn't walked away from it never to think about it again.

An example, and I think a very good example, is the Winston Select product that you referred to earlier, where that's an attempt to come back and employ all the design techniques that we can and still maintain consumer acceptance we think and

reduce as many of the constituents that have been pointed to as potential problems in one product.

And so the tobacco-specific nitrosamines was one of the reduction goals, along with carbonyls, along with nitric oxide and a variety of others.

So if I understand what you were asking, we haven't just addressed one constituent and then somebody in the scientific community says, oh, we don't think that's the problem, so we just move on never to look back, never to continue that kind of research.

Q. Because that's not true, sir, is it? The scientific community hasn't identified benzo[a]pyrene, for instance, and then Reynolds worked on it, and then the scientific community said, oh, we were wrong; that didn't happen, did it?

A. I'm not sure I understand your question.

Q. Well, the scientific community has not moved away from benzo[a]pyrene as being a dangerous substance in cigarette smoke ever since it was identified in cigarette smoke up until this day; isn't that true?

A. Let me try to answer that question by giving my perspective of the bigger picture. I think toxicologists and medical researchers in days gone by

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looked at the problem of cigarette smoking as the silver bullet theory. There is something in cigarette smoke that is causing the problem, causing this association with diseases.

And, you know, and so they looked at it as a silver bullet. If you remove this one thing or this one class of compounds, we would probably be all right, wouldn't we? And then as toxicology has developed, I think people have understood that in very complex mixtures, like cigarette smoke, and many other complex mixtures, the silver bullet approach probably doesn't make a whole lot of sense because what really matters is the combination of many constituents often present at low levels, and that combination, in fact, in that complex mixture may be important.

So I think toxicology has evolved. So back in the '50s, certainly, everybody seemed focused on the silver bullet approach. Today, and for a number of years, because toxicology and medical research has evolved, I think that research as well as research at Reynolds has focused on reducing a broad range of many constituents. There is no silver bullet.

Q. All right. And now let me see if I can

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restate my question and see if we understand each other.

It has never happened, has it, that scientists identified benzo[a]pyrene years ago as a dangerous substance in cigarettes and then subsequently said it wasn't a problem? That's never happened, has it?

A. What scientists did in the early '50s was said, we think benzo[a]pyrene could be or is the problem, depending on who you talked to. At some point a few years later, scientists then said, wait a minute. We now know how much benzo[a]pyrene is present in cigarette smoke, and it's insufficient to account for the mouse skin painting results.

Therefore, there must be something else going on, like phenols as promoters acting synergistically with benzo[a]pyrene that may account for the mouse skin tumorigenicity.

Then in the end, they concluded, well, gee, that's still not sufficient and there is probably other things, so they moved on to other things. But, no, to your point, scientists then didn't just throw benzo[a]pyrene away as a viable or a constituent of concern. That constituent still remains on the surgeon general's list as one of

concern, it remains on the IARC list as one of concern, and it remains on the Reynolds' list as well.

Q. And you said that scientists identified these substances. Reynolds' scientists never identified these substances first, did they?

A. I'm not sure that's fair. We did, in fact, identify a number of polycyclic aromatic hydrocarbons in smoke. Whether we were the first, we were certainly right in there near the first.

Q. Which ones?

A. Well, there is a list of them. I can't recall which ones came first and which ones came after. Benzo[a]pyrene, however, because it's of the polycyclic aromatic hydrocarbons, is present in the largest concentrations. That was one of the first that we identified in smoke and quantitated in smoke.

Q. All right. One of the first that you identified in smoke. What are you talking about, benzo[a]pyrene?

A. Benzo[a]pyrene.

Q. You're not saying Reynolds identified benzo[a]pyrene first as a toxic constituent of smoke, are you?

A. That's not what I said.

DAVID E. TOWNSEND, Ph.D. - EX. BY MR. WESTBROOK

Q. All right. I want to understand that.

A. Yeah, that's not what I said.

Q. All right. Can you name for me one polycyclic aromatic hydrocarbon that Reynolds identified and published first in the peer reviewed scientific literature? Just give me one.

A. Well, I can't off the top of my head. I think we have to go back and look at the records and have to go back and look at the detailed research studies.

Reynolds has identified and quantitated a large list of polycyclic aromatic hydrocarbons. They have presented a lot of that research, and they have published a lot of that research and even presented it at the American Chemical Society meetings. So -- but I can't tell you as we sit here today without us going back and looking at detailed research records exactly when various compounds were identified and quantitated and whether, in fact, they were the first recordings of such identification.

Q. Now, is it your view, sir, from what I understand you having said before, that epidemiologic investigation does not prove that smoking causes cancer? Is that your view?

A. That definitely is my view. I believe

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epidemiology is a valuable area of science that points directions for additional work.

Q. All right.

MR. WESTBROOK: Let's mark as next an article from the February 7th, 1959 edition of the British Medical Journal by Dr. Ernst Wynder.

(PLF. EXH. 15, Article from the British Medical Journal dated 2/7/59 entitled "Laboratory Contributions to the Tobacco-Cancer Problem" by Ernst L. Wynder, M.D., was marked for identification.)

BY MR. WESTBROOK:

Q. And, Doctor, you are free to look at whatever you want, but I'm going to ask you about the introductory section where he reviews the types of research that can be done and specifically about the role of epidemiology.

A. Okay. I've skimmed the introduction section.

Q. Okay. And let me ask you the question. If you need to look at more, you certainly can. But my question really concerns the introduction rather than this particular study.

Is it true that in 1959 Dr. Wynder, who I

think you described as an excellent scientist, said there, quote:

The importance of laboratory work is not to prove that smoking is a cause of cancer in man, period. Such proof can only come from human epidemiological investigation, unquote?

Did he say that, sir?

A. Well, that's what he said here.

Q. Is this the same Ernst Wynder who you know to be one of the leading tobacco researchers at least in this country?

A. Well, this is the same Ernst Wynder that I said I regarded as a good scientist, no question.

Q. All right. And Dr. Wynder said that the proof that smoking causes cancer can only come from human epidemiological investigation; isn't that right?

A. That's what he said here, yes.

Q. And you disagree with Dr. Wynder?

A. Again, I'm not an expert in epidemiology. My superficial understanding of epidemiology is that in a retrospective study, in other words, if we conduct a retrospective study and that in effect determines or can determine what factors may be associated, then that points the way

for additional research. For example, the genetics research that's going on now is very exciting and ways to look at how cigarette smoking may cause cancer is making great advances.

But the retrospective epidemiology doesn't, in my mind, to my limited understanding, define proof or define causation. A 30-year prospective study, if it's done right, may. I don't know. And maybe that's what he is referring here to.

Q. All right. And Dr. Wynder, according to this article, said almost 40 years ago that epidemiology is the way to find the proof whether smoking causes cancer or not; that's what he said?

A. But again, I don't know exactly what he is referring to. Is he talking about a highly controlled 30-year prospective study? Is he referring to the existing retrospective studies that existed as of 1959? I don't understand that.

And also, he didn't have the benefit of our present state of knowledge about genetics research.

Q. Has R. J. Reynolds ever conducted an epidemiological study to investigate the connection between smoking and cancer?

A. We have some people at Reynolds who are

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very knowledgeable and quite knowledgeable on epidemiology. I'm not aware that we've ever conducted epidemiological research, however.

Q. Has R. J. Reynolds ever supported Dr. Wynder or any other epidemiologists in conducting an epidemiological study on the relationship between smoking and lung cancer?

MR. McDERMOTT: Objection. No foundation.

THE WITNESS: I don't know.

BY MR. WESTBROOK:

Q. Have you ever seen the results in the RJR technical library or anywhere else floating around the company of any epidemiological study that Reynolds supported on smoking and health?

A. Or any epidemiological research?

Q. Yes.

A. I have never seen such results conducted by Reynolds.

Q. Doctor, don't you think that a company that is selling billions of cigarettes a year for decades and decades has an obligation to support studies like epidemiological studies on smoking and health matters?

MR. McDERMOTT: Objection. No foundation

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and assuming facts not in evidence.

THE WITNESS: Reynolds has supported a lot of outside research, medical research, university research. It's not clear to me that supporting epidemiological research is necessarily the best way to go. A lot of epidemiology exists.

Nobody doubts that cigarette smoking is a risk factor. No question about it. It's unclear to me, again, superficially, as a layman, that conducting a lot of additional epidemiological research is necessarily the best way to advance the ball.

However, university research, medical research may be. And I know Reynolds has put a lot of money into that.

BY MR. WESTBROOK:

Q. How much money has Reynolds put into that?

A. Quantitatively, I don't know. It's a lot.

Q. According to this 1990 R. J. Reynolds letter that we looked at, which is exhibit 14, as of 1990, Reynolds was telling a school principal that the entire tobacco industry had given over $162 million to research over the years. Did I

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summarize that accurately?

A. It says over the years, the tobacco industry has given in excess of 162 million to independent research on the controversy surrounding smoking.

Q. All right. And that's the same tobacco industry that in just that one year, 1990, spent almost $4 billion to advertise; isn't that right?

A. I don't know what the advertising budget was for the industry in 1990.

Q. Let's look at the advertising budgets as the industry reported it to the government for a minute.

MR. WESTBROOK: Let's mark as next the 1994 report of the tobacco industry to the Federal Trade Commission.

(PLF. EXH. 16, Document entitled Federal Trade Commission Report to Congress for 1994, was marked for identification.)

BY MR. WESTBROOK:

Q. And, Doctor, to assist your review, I'm going to reference page 18, which is the report for the year -- contains the report for the year 1990 on the industry's advertising budget.

A. Page 18?

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Q. Yes, sir. Upper left-hand corner for 1990.

A. Sorry. I'm just trying to get a quick sense of what this document is.

Q. Doctor, take all the time you need, sir.

MR. McDERMOTT: His need for time is in preface to my objection to this line of questioning, which is no foundation. This witness is being offered for his expertise in cigarette design and chemistry, not advertising or government reports or anything of this sort.

THE WITNESS: Okay, I've just quickly scanned it, and I'm on page 18.

BY MR. WESTBROOK:

Q. All right. Do you see, sir, in the upper left-hand corner the listing for 1990 for domestic cigarette advertising and promotional expenditures?

A. I see at the top of the page, domestic cigarette advertising and promotional expenditures for years 1990 to 1993.

Q. All right. And then in the left-hand column at the top, the year 1990 is listed?

A. That's correct.

Q. And at the bottom the total for 1990 is $3.9 billion?

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A. That's correct.

Q. All right. So in one year, 1990, the same tobacco industry whom Reynolds told a principal had spent 162 million over the years in research had spent 3.9 billion in that year alone on advertising; is that correct?

MR. McDERMOTT: Object to the form of the question. No foundation.

BY MR. WESTBROOK:

Q. Is that correct, sir?

A. That's what the table shows.

Q. All right. And is it apparent to you, sir, that the amount the industry is spending on advertising dwarfs the amount that it spends on research?

MR. McDERMOTT: Object to the form of the question. No foundation.

THE WITNESS: If I accept these numbers as true, the advertising expenditure estimate in this document, of course, is far larger than $162 million as indicated by the other document.

BY MR. WESTBROOK:

Q. All right.

A. The other document does go on to say that this value of 162 million is more than all the

51676 0209

voluntary health associations combined.

Q. And where do you think the voluntary health associations have to go to get their money?

A. I have no idea.

Q. Well, the American Health Foundation, which is a health association, doesn't get any money from Reynolds, does it?

MR. McDERMOTT: Object. No foundation.

THE WITNESS: I'm not aware of research contracts that have been granted to the American Health Foundation by Reynolds. I don't know.

BY MR. WESTBROOK:

Q. Doctor, let's mark as next the RJR fourth quarter annual report for -- dated January 1997. I'll mark that as the next exhibit in order.

(PLF. EXH. 17, RJR Nabisco Fourth Quarter Report dated 1/28/97, was marked for identification.)

BY MR. WESTBROOK:

Q. Doctor, I think you said before you are a Reynolds' shareholder, correct?

A. I have some Reynolds' stock.

Q. All right. And as a shareholder, you get the annual reports and quarterly reports from the company?

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A. Yes, I do.
Q. Have you seen this particular quarterly report from Reynolds dated January 28th, 1997?
A. Yes, I received it.
Q. Okay. Turn over to the last page, sir, which reports the results for the three months ended December 31st -- excuse me, the 12 months ended December 31st, 1996, the next to the last column.
A. All right.
Q. All right. And do you see under net income that the company reported that in 1996 it earned $1.76 billion?
A. Where do you see that?
Q. Is that 1.7 -- do you see under net income three lines up from the bottom?
MR. McDERMOTT: That's per share.
THE WITNESS: That is per share.
BY MR. WESTBROOK:
Q. Oh, it's $1.76 per share?
A. Per share.
Q. Can you tell me where the net income is, sir? Is that 580 million?
A. I would believe that's right. I'm no finance expert.
Q. Can you recollect for me, sir, what the

51676 0211

research budget was for your group in 1996?

A. The total R&D budget in 1996 was approximately 66 or 67 million.

Q. And how much of that budget went to tobacco and health research?

A. I can't give you a specific number. Some of that money did go to tobacco and health-related research; however, funding of additional smoking and health research, for example, comes from other parts of the company budget as well, not just from the R&D budget.

Q. Okay. Do you have in mind a number which would be RJR's total contribution to the tobacco health research in 1996?

A. No, I don't.

Q. Do you have an estimate?

A. No.

Q. Do you know how much of your budget of $66 million went to tobacco health and research?

A. Of R&D's budget?

Q. Yes.

A. No, I really don't.

Q. Do you play any role in deciding how much of the R&D budget goes to tobacco and health research?

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A. A minor role. Mostly in helping decide which projects to fund, some projects to fund, some not to fund. Again, it's separate from a lot of the contracts or the grants that are given to academic and medical research. A lot of the medical research or smoking and health-related research in the R&D budget is, in fact, focused on specific projects, specific questions about smoking and health.

Q. Do you have a feeling whether the R&D budget devoted as much as 10 percent of its budget to smoking and health research?

A. Again, I can't -- I can't estimate what fraction of that budget was smoking and health related. It also depends in large part on how you define smoking and health research.

Q. Am I correct that you have sat in on meetings where it's been decided what programs the R&D budget should go to fund?

A. The group of us, the R&D executive group, in fact, reviews projects. We recommend the formation of new projects. We recommend the discontinuing -- the discontinuation of some projects. We provide technical review of a variety of projects and help decide how best to use -- to use our limited resources.

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Q. Now, who was in the R&D executive group?

A. Well, the vice president of R&D, of course, leads that group.

Q. Who is that?

A. That's Dr. Gary Burger.

Q. Okay. Who else?

A. Oh, you want the full list?

Q. Unless it's 50 people long.

A. It includes the R&D directors and that includes Dr. Debethisy, Dr. Suber, Mr. Willard, and Ms. Wheeler, Mr. Phillips, Mr. Tinsley and myself. I believe that's a complete list.

Q. All right. What do you call the document which directs how the R&D budget is to be spent each year?

A. There is not one document per se. We're responsible for effectively using our limited resources for the company. And in the course of that, we will sit down and look at existing projects, review those independently. Some of them we will review together as a group collectively as a group of projects. There is not one structure, not one document that clearly outlines it.

This is an iterative process that we conduct. We start out at budgeting time, lay our

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best estimates; and as the year goes on, we continually refine those estimates and make changes as we need to. So I can't point you to one specific document. There is not one specific hard-and-fast protocol of how we do it.

Q. What types of documents are these decisions memorialized in?

A. Well, some of the information is in R&D memoranda. Some of it is in project report -- status reports. Some of it is just in tabular data or graphic representation of various aspects of budget and project management that are not necessarily formal memoranda. So it's just a variety of things.

Q. Does the R&D Department prepare a year end report on how the department spent its money in the previous year?

A. We have a complete budget at end of year, and we can define how money is spent in the previous year.

Q. And what do you call that document?

A. The R&D budget.

Q. Does that budget look forward to the next year as well as reviewing the previous year?

A. We have a separate budget for each year, of course. And we develop -- while one year is going

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on, toward the end of that year, we will develop a proposed budget for the following year. And, again, it's a changing budget, a changing document.

Q. Well, I understand that a budget would be developed for the coming year, but is there a document that memorializes how the money actually had been spent in the previous year such as a summary or recap?

A. That's what I'm saying. At the end of the year, there is a budget breakdown that lists our entire actual expenses.

Q. A final budget as to how the money was really spent?

A. That's correct.

Q. Okay. And that's done for each year?

A. Yes.

Q. You are the director of product development. What is Dr. Debethisy's role?

A. He is in charge of biochemical and biobehavioral research.

Q. Okay. Did you say Dr. Suber?

A. Yes.

Q. What is Dr. Suber in charge of?

A. He is in charge of health and regulatory sciences, primarily a group of toxicologists.

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Q. How about Mr. Willard?

A. Process engineering.

Q. What is process engineering?

A. Developing and modifying processes.

Q. Processes for the manufacturing of cigarettes?

A. For cigarettes, for tobacco, primary processing, cigarette manufacture, packaging, a variety of things.

Q. Does that include the development and the processing of reconstituted tobacco?

A. Modifications to that process or development of new processes. The current process is the responsibility of the Operations Department.

Q. Let me ask you about reconstituted tobacco for a minute. Is it correct that reconstituted tobacco is a process by which your company takes material that it previously couldn't use in a cigarette and combines it into a form to where it can then be used in a cigarette?

A. That's close.

Q. I'm doing well then.

A. What the reconstituted process was originally developed for was because we had pieces of tobacco that were too small to make good cigarette

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rods. They were too small to go through the cigarette maker. They were waste material. The reconstituted process was developed to take those small pieces, prepare a sheet, which is then cut into larger pieces that could be effectively used in cigarette manufacture.

Q. So Reynolds found a way to use the waste material then in cigarettes?

A. The waste material meaning pieces that are too small from the stemming operation, so it not necessarily is considered waste tobacco per se but the pieces are just too small. It may be pieces of lamina, good leaf material. Also it allows the use of stem. It allows the use of very small pieces of tobacco which we sometimes call tobacco dust.

Q. All right. Before the reconstituted tobacco process was put into use, is it correct that the ingredients of reconstituted tobacco were all thrown out?

A. By and large that's true, yes.

Q. So the reconstituted tobacco process really was an economical way to use material that otherwise would have been discarded?

A. No question about it. The driving force for the development of reconstituted tobacco

initially was economics.

Q. Okay. Am I correct in a general way that reconstituted tobacco is made and in one of the steps the nicotine is removed from the mixture during processing?

A. Well, a group of water solubles are removed, and nicotine is in that as a water soluble.

Q. All right. And then at some point, is nicotine put back onto the reconstituted tobacco sheet?

A. That's correct. It's put back onto the pulp sheet that's formed, and the resulting pulp sheet with the extract reapplied, with the water soluble material reapplied, then becomes the reconstituted tobacco.

Q. Is the same nicotine that's taken out of a batch early in the process put back onto the sheet later on?

A. We have a -- we have a closed system, and so what comes out goes back on. Now, it may not -- it depends on how microscopic you want to look at it. If you take one little section of tobacco sheet and say, does that specific nicotine come from that specific fiber of tobacco, the answer is probably no, because the overall process, of course, averages out

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everything. But what goes in comes out.

Q. So going into the process will be pieces and stems of various types of tobacco that would have varying nicotine contents, I assume?

A. That's right. The small pieces of tobacco lamina would generally have somewhat higher nicotine levels than stems. Stems typically have low nicotine levels. So the in-feed materials do have different nicotine levels.

Q. And what is the design characteristic of the nicotine that's sprayed back on the reconstituted sheet?

A. I don't understand what you mean design characteristic.

Q. Well, is there a percentage or weight of nicotine that is sprayed on per square foot of sheet?

A. No. What comes out, what is extracted is reapplied, and that will vary depending on the in-feed materials. I think the other thing that happens is in the course of processing, extracting the water solubles from the tobacco materials, making the paper sheet, reapplying those water solubles, in that process, there is nicotine and other water solubles lost.

So there is a slight reduction in total

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nicotine because of manufacturing losses. But ...

Q. What I'm trying to understand, is there a design characteristic for the amount of nicotine that you want to have on that sheet that comes out?

A. No. There is a design characteristic for the types of materials that we can make good reconstituted sheets. For example, stems, the use of stems, because of the long fiber size, gives fairly good sheet properties and a fairly strong sheet that we can then handle and cut to the right size fairly well.

So there are a portion of stems, tobacco dust and maybe small pieces from the stemmery that are the right types of proportion to make good reconstituted sheets. But to your specific question, is there a design application rate for reapplying, the answer is no.

Q. All right. Is there a feed rate for the liquid to be sprayed onto the sheet?

A. Well, the reapplying the water solubles, of course, requires doing it right. You've got to monitor the spray rates. You've got to have the right kind of nozzles and everything to make it all work out right because you don't want to wind up short and have reconstituted pulp sheets and you've

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used up all the extract and have none to apply to it.

And the other thing is you don't want to run over, either. You don't want to have the application rate lower so that you wind up with excess water solubles. You want to reapply the water solubles at the same rate that the paper sheet, the pulp sheet, is moving through the process to make everything work out right.

Q. Can the application rate of the nicotine and the other solubles be varied?

A. Oh, of course.

Q. And that's an area that Mr. Willard would know much more about, I assume?

A. Mr. Willard is responsible for process engineering. He knows a lot about reconstituted tobacco.

Q. All right. Now, how about Ms. Wheeler; what's her area of expertise?

A. She is responsible for a variety of things, including R&D planning, R&D facilities, and support services. For example, the library, computer support -- the computer support group and the physical plant.

Q. All right. How about Mr. Phillips, what

is his responsibility?

A. He is responsible for Eclipse product development.

Q. And how about -- is it Mr. Tealey?

A. Tinsley.

Q. Can't read my writing. What is Mr. Tinsley responsible for?

A. He is -- he is responsible for existing brands support, R&D support, and existing brands product development.

Q. And among that group, when y'all get together, you somehow or other divide up the R&D pie; is that a layman's way of saying it?

A. I think that's fair.

Q. All right. Do you also as a group make applications to management to increase or decrease your R&D budget for the following year?

A. We make a variety of arguments to management, not only to Dr. Burger as head of R&D, but also to the executive committee downtown. We make arguments to make sure they have the benefit of our thoughts about how R&D can best help the company and the kinds of research that we need to be providing for the company.

In some cases, those recommendations are

accepted, and sometimes they are not, so I think just like any department in any industry, we have to make rational, reasonable arguments for the types of R&D efforts that we think make sense.

Q. Let's just look back at the last couple of years. Has your R&D budget increased significantly over the last couple of years?

A. Our R&D budget has been reduced significantly over the last number of years.

Q. All right. When did the reduction in the R&D budget begin?

A. Well, it's hard for me to say exactly. R. J. Reynolds' sales and share of the market has been declining, and consequently, all departments in R. J. Reynolds have been cutting back, and our budget has been cutting back pretty gradually over a number of years. I would say, if I had to pick a time when it started reducing, when the company reduced the budget seriously was probably beginning in '91, '92, that period, and it's been a gradual reduction since.

Our R&D budget is directly tied to our share of the market and our earnings.

Q. Is it your understanding, sir, that your R&D budget has been reduced by the same percentage as

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the advertising budget?

A. I don't know how the relative reduction percents compare. I haven't done that analysis.

Q. Do you see figures that show the RJR advertising budget for the year?

A. I've seen them before. I can't say that I routinely see them.

Q. I assume you don't have the exact numbers in mind, but is it a fair assessment that the advertising budget within RJR for tobacco products is very much larger than your R&D budget?

A. Well, it's hard for me to quantitate very much larger. My estimate -- and again, this is off the top of the head -- my estimate is that it's larger. The marketing budget has suffered major cuts, major reductions, but I can't quantitate very much larger. You know, it may be two or three times larger or four times larger than our R&D budget as opposed to 100 times larger. But I can't give you a quantitative estimate.

MR. McDERMOTT: Is this a good time to take a short break?

MR. WESTBROOK: Sure.

THE VIDEOGRAPHER: Okay. This concludes tape 3. The time is 3:36 PM.

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(A recess transpired.)

THE VIDEOGRAPHER: This is the continuing deposition of David Townsend in the case of The State of Florida versus the American Tobacco Company. This is the beginning of tape number 4. The date is May the 29th, 1997. The time is 3:48 PM. Counsel.

BY MR. WESTBROOK:

Q. Dr. Townsend, we spoke a little bit earlier about nitrosamines. When were nitrosamines first identified by Dr. Hoffmann who you talked about or others as a dangerous component of cigarette smoke?

A. Tobacco-specific nitrosamines, I believe, were identified in the mid -- mid '70s or thereabouts. As -- they were identified as tobacco constituents at that time.

Q. And how about the nontobacco-specific nitrosamines?

A. Some of the nontobacco-specific nitrosamines were identified somewhat earlier, I believe.

Q. In the 1960s?

A. Back in the '60s, yes, sir.

Q. And as I understand what you said earlier, Reynolds has developed a Winston Select

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which uses a tobacco type which reduces the nitrosamines in tobacco smoke; is that right?

A. It uses a proprietary blend that does effect some reduction in some of the tobacco-specific nitrosamines.

Q. And when was that product with that special blend first available commercially?

A. We launched it in the Oklahoma test market -- it's hard for me to remember exactly when -- in the neighborhood of two years, two and a half years ago.

Q. Prior to the launching in that one market of the Winston Selects with reduced nitrosamines, had R. J. Reynolds marketed any brand of cigarettes that had reduced nitrosamines?

A. We've done a lot of research on ways to reduce tobacco-specific nitrosamines, and until the Winston Select, I don't believe we've effected -- been able to effect a significant reduction. We do know a lot more about the formation of tobacco-specific nitrosamines, and we're researching ways to effect a bigger reduction at this point.

Q. Now, the way you're marketing this Winston Select with reduced nitrosamines, do you communicate that fact at all to the consuming smoking

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public?

A. We have not communicated that to the consumers in Oklahoma. We have communicated that to the scientific community in the form of publications and presentations at scientific meetings and at presentations to, for example, the special committee formed by Health Canada. So there have been a variety of disclosures to the scientific community, not to the consumer.

Q. All right. So if I'm a consumer in Oklahoma, and I see a package at the 7-Eleven that says Winston Select, why should I want to try it?

A. Well, there are other benefits to that product, as well. One, because of the very special carbon filter, we're able to retain good taste characteristics and reduce a lot of the harshness and irritation from cigarette smoke. So it is a very mild product with reduced irritation.

Those are benefits that the consumer can very easily perceive.

Q. All right. Do you advertise Winston Selects as a healthier cigarette?

A. We don't advertise it as a healthier cigarette in spite of the fact that it does have reduced chemistry. We don't know, and there is

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really frankly no way to prove, whether it's safer than other cigarettes or not so that there is a difference in biological end points.

Q. Do you accept it as true that some smokers are concerned about their health and their continued smoking?

A. I believe that -- that cigarette smokers are aware that cigarette smoking is a risk factor. No question in my mind about it. I also believe that cigarette smokers, many cigarette smokers, in fact, would like a cigarette that potentially has reduced risks.

Q. If I were out in Oklahoma, and I saw Winston Selects, and I called the hot line number, assuming I could get through, is there someone on that hot line who would tell me that Winston Selects have reduced nitrosamines?

A. I think that's unlikely and for a very good specific reason.

Q. Is the reason that you don't think people would understand what they are saying, what they said?

A. No, I don't think that's the reason at all.

Q. All right. Do you believe saying that

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Winston Select has reduced nitrosamines is equivalent to making a health claim for the product?

MR. McDERMOTT: Does he believe personally?

THE WITNESS: You're asking me personally? Are you asking my personal opinion?

BY MR. WESTBROOK:

Q. I'll ask personally first, and then I'll ask whether there is a difference if you're sitting here as an R. J. Reynolds' employee.

First, as your personal opinion, do you believe that telling somebody that a cigarette has reduced nitrosamines is the equivalent to making a health claim for the product?

A. My personal opinion is that I don't believe that making statements about the chemistry reductions necessarily constitute a health claim. I think that it is what it is. And, again, I think I've made it clear that I don't believe there is any way to demonstrate whether there is an overall reduction in health risk as a result of that. There should be. You would expect it to be, but there is no way of proving it. That's my personal opinion.

Q. All right. Now, do you have a position as a research director at R. J. Reynolds concerning

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that?

A. I would love to tell consumers that that product has reduced nitrosamine levels and reduced carbonyl levels and reduced free radicals and reduced nitric oxide and reduced -- and we can go and on and on. And I would like to be able to tell them that, by the way, that product has shown some reduction in several biological measures in the laboratory.

But, unfortunately, the FTC would regard those as implied health claims. Even speaking to reduced chemistry, the FTC is clear that that would be an implied health claim, and they would go after that product.

Q. All right. And is the reason to your knowledge why the FTC prohibits the tobacco companies from making health claims that because in years past, the industry abused its right to speak and made health claims -- made health claims that were not supported by the scientific evidence?

MR. McDERMOTT: Object to the form of the question. No foundation. Assumes facts not in evidence. If you can answer it, you may do so.

THE WITNESS: My opinion is, I don't believe that to be the case at all. I believe that the FTC, like they would in other industries, they

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look at two very careful parts of advertising, and that's explicit claims, and a company needs to be able to substantiate explicit claims; and if there are implied health claims, they need to be able to substantiate those implied health claims as well.

It's easy to substantiate explicit claims of reduced chemistry. As I said, I don't know of any way to substantiate an implied health claim of reduced risk. So if that's the implied health claim and that's what the FTC judges a reduced chemistry claim to be, and there is no way to prove that it, in fact -- that it meets that implied health claim, the FTC would enjoin that product.

BY MR. WESTBROOK:

Q. Has Reynolds to your knowledge approached the FTC and asked for permission to state if it's true that Winston Select has reduced some nitrosamines?

A. I'm not aware of such a meeting.

Q. Now, is it true that Winston Select actually has an increase in some nitrosamines over conventional cigarettes?

A. What do you mean over some conventional cigarettes?

Q. Well, over other Winston brands, that

nitrosamines are higher in Winston Selects than they are in other brands that Reynolds sells?

A. That's not the basis of comparison. The basis of comparison is with other products that have the same tar level.

Q. Okay.

A. Because nitrosamine levels vary in proportion to the tar level in general. So there are ultra low tar products, for example, that have lower nitrosamine levels than Winston Select. But for an equivalent tar level of roughly say 10 milligrams per cigarette for that product, it shows substantial reductions in some of those nitrosamines compared to other products at 10 milligrams.

Q. And compared to other products at 10 milligrams, are there some nitrosamines for which Winston Select has a higher number than those other 10-milligram products?

A. Of those that are reduced, I'm not aware that they are higher than any other 10-milligram product. I don't recall ever seeing nitrosamine data that shows Winston Select to be higher than any other 10-milligram product.

Q. Okay. Now we've talked some today about benzo[a]pyrene. Can we refer to it as B[a]P to save

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some transcript space? Will you understand what we mean?

A. Sure.

Q. Okay. I saw some testimony that you gave previously comparing the amount of B[a]P in cigarette smoke with the amount of B[a]P in a broiled steak.

Do you remember giving some testimony along those lines?

A. Yes, I do.

Q. And I think the testimony was that you -- that one eight-ounce steak was at the equivalent of 600 or so cigarettes?

A. One charcoal-broiled steak, yes.

Q. One charcoal-broiled steak. Okay. Did you do that calculation?

A. I did that calculation actually from data that's in an elementary chemistry book. It's actually an organic chemistry book, first level.

Q. And what book did you use?

A. The author is Noller. It's actually a very old text. It's not one of the more common organic texts in use in universities, but anyway, it's actually an outstanding textbook.

And in that text, there is discussion about benzo[a]pyrene levels, and there were analyses

reported of benzo[a]pyrene levels in charbroiled steaks.

Q. And how do you spell Noller?

A. N-O-L-L-E-R.

Q. And do you know the title of the book?

A. Organic Chemistry.

Q. Where did you get the book, sir?

A. The university.

Q. All right. And in that book, you found a number for the amount of benzo[a]pyrene in a charbroiled steak?

A. That's correct.

Q. Okay. And then you needed a number for the amount of benzo[a]pyrene in a cigarette, right?

A. That's correct.

Q. Where did you get that number?

A. From R. J. Reynolds.

Q. All right. And what number did you use for the amount of benzo[a]pyrene in a cigarette?

A. I can't remember exactly. I would have to go back to my notes, but I can tell you what typical levels are now.

Q. Okay. Tell me what the typical levels are.

A. Well, the typical levels now are five to

seven nanograms per cigarette. But, again, it varies a lot depending on the tar yield of the product, with ultra low tar products delivering proportionately the same reduction as the tar.

Q. Now, the five to seven nanograms of benzo[a]pyrene per cigarette, is that the entire range of benzo[a]pyrene delivered by Reynolds' cigarettes or is that a subset of the range?

A. No. No. I said that's typical for a full flavor product.

Q. Full flavor would be five to seven nanograms?

A. Typically.

Q. So seven nanograms would be the highest nanogram reading you would expect in the full flavor cigarettes sold by Reynolds?

A. I said that's a typical range. I don't know that that's the highest but that's a typical range of full flavored products.

Q. Okay. All right. Okay. So then that's five to seven nanograms delivered by smoking one cigarette?

A. That's five to seven nanograms per cigarette.

Q. Per cigarette, all right. And that is

benzo[a]pyrene that's inhaled, correct, or inhalable?

A. Inhalable, presented to the smoker.

Q. All right. Are you a vegetarian, sir?

A. No.

Q. All right. Do you eat steaks?

A. Occasionally. Not often.

Q. Did your organic chemistry book tell you where the benzo[a]pyrene in a steak that is barbecued is located?

A. There was a brief discussion about it and about the process of formation of benzo[a]pyrene in the fat in long chain waxes, in fact, fall from the steak onto the hot coals. Benzo[a]pyrene is formed in that pyrolysis process. The smoke or aerosol from that then deposits the benzo[a]pyrene back on the steak.

Q. So when you have your number of benzo[a]pyrene on a steak, you are not talking about the amount that somebody breathes hanging over the grill; you are talking about actually what's on the surface of the steak?

A. What I've been talking about is what's on the surface of the steak. If you breathe the smoke from a barbecue grill, I would assume you would get benzo[a]pyrene there as well.

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Q. Do you know what level it would at?

A. No.

Q. All right. So you were comparing the benzo[a]pyrene on the surface of a steak with benzo[a]pyrene in the aerosol smoke from a cigarette; is that right?

A. That's correct.

Q. Okay. And I take it we can agree that nobody inhales steaks? They may eat them quickly, but they don't inhale them?

A. I think in practice that's correct, although the terminology sometimes is used.

MR. McDERMOTT: We'll give you that one.

BY MR. WESTBROOK:

Q. All right. All right. And nobody, at least in their right mind, eats a cigarette; is that right?

A. I don't know of many people that eat cigarettes.

Q. All right. So you were comparing in this testimony benzo[a]pyrene formed on the surface of an item that was to be eaten with benzo[a]pyrene which came out in the smoke of an item that was being smoked; is that accurate?

A. That's fair.

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Q. Okay. And the benzo[a]pyrene from smoke would normally impact on what organs in the body?

A. Well, the lungs, the respiratory tract in general.

Q. All right. And unless you have a particularly unfortunate incident while eating, it's unlikely that a piece of steak is going to go into your lungs; is that right?

A. I would certainly hope not.

Q. Hopefully the steak will go down into the stomach and into the gastrointestinal tract, right?

A. (Moves head up and down.)

Q. Are you familiar with the differences in the way that the body chemistry reacts to inhaled materials versus ingested materials?

A. No, I'm not.

Q. All right. Do you know what the body does to benzo[a]pyrene that's eaten and digested in a steak?

A. No. I'm not an expert in that area.

Q. All right. Do you have any basis to say that the amount of benzo[a]pyrene that's on an eight-ounce steak is more or less dangerous to a person eating it than the amount of benzo[a]pyrene that's in the 600 cigarettes that you talked about in

your testimony that's inhaled?

A. I don't recall ever making any statement nor coming to any conclusion myself about the relative danger. I think all I was trying to demonstrate was that benzo[a]pyrene is present in a number of things and sometimes in fairly high levels compared to that presented from cigarettes. That's all. I don't know what the relative risks are, what the relative biological significance is.

Q. But the level at which it's present in cigarettes is present in a different form than it is in a steak, isn't it?

A. Certainly. Certainly. I don't know what impact that has.

Q. Wasn't it a comparison of apples and oranges to compare a steak to a cigarette?

A. Again, all I was trying to do was show that there are exposures from other means, that cigarette smoke, while it contains benzo[a]pyrene, is not alone, that there are other exposures. I wasn't trying to make any relative judgment of risk or anything of the sort. And if you take it to be an apples-and-oranges comparison, well, then so be it.

Q. Do you know of any study ever showing that someone has gotten lung cancer from eating

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Source: https://www.industrydocuments.ucsf.edu/docs/tggl0001

charbroiled steaks?

A. I have no idea.

Q. You don't know of any such study, do you?

A. I've never seen such a study. I have no idea. Again, I'm not an expert in the area. I don't know what any health implications of benzo[a]pyrene on steaks, you know, may be.

Q. Now, you did another comparison that I saw in one of the transcripts, and I would like to mark this as next, apparently comparing the amount of benzo[a]pyrene in smoke to an Equal packet.

Do you remember that comparison?

A. Yes.

MR. WESTBROOK: Let's mark that as next.

(PLF. EXH. 18, Comparison document comparing BaP in Winston cigarettes to Equal, was marked for identification.)

BY MR. WESTBROOK:

Q. Do you recognize this chart as a chart that you prepared and testified about at a previous trial involving smoking and health?

A. Yes.

Q. Okay. Did you prepare the chart?

A. Yes.

Q. Okay. Did you get the packet of Equal

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and put it on the page and photocopy it like that?

A. No, our graphics art people did that.

Q. They did a nice job. And now on this chart, you're comparing the smoke from cigarettes to the contents of a packet of Equal, as I read the chart; is that correct?

A. The purpose of this chart was to try to demonstrate to a jury who may not have a background in science or a background in -- or any way of looking at these very low quantities easily, and it was for -- just to demonstrate that -- that the benzo[a]pyrene in cigarette smoke is a minuscule quantity, very small, very small level. That's the point of the analogy to the pack of Equal so that people in their mind could grasp kind of what weight, what size of material we are talking about and then relate that back to the nanogram level.

Q. Are you saying -- and I see that the Equal chart and the record will show it, indicates that there is a pile of material below the Equal packet that's been poured out. Were you attempting to indicate that that was the amount of benzo[a]pyrene that would be in 100 million Winston cigarettes? Is that what you're saying?

A. All I was trying to do was use this to

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help the jury understand that benzo[a]pyrene levels in cigarette smoke is extremely small. And that to -- for a rough approximation, that roughly to equate to -- if a cigarette delivered 10 nanograms of benzo[a]pyrene per cigarette, that to get enough benzo[a]pyrene to be equivalent in weight to one Equal packet would require about 100 million cigarettes to be smoked.

Q. All right. It certainly, sir, is much more dangerous from a toxicological point of view to have 100 million doses of benzo[a]pyrene at ten nanograms than to have one Equal packet dose of benzo[a]pyrene; isn't that right?

A. I wasn't trying to make any arguments about risk, danger, health or anything. All I was trying to do was make this a comparison. Because, again, nanograms, micrograms, these small quantities, these small measures are extremely hard for people to wrap their heads around unless you deal with those kind of numbers every day. That's the only point of this exhibit.

Q. Let me ask my question and see if we can understand it and maybe get an answer.

Is it correct, sir, and do you know from your experience, 20 years in tobacco research and

from whatever reading you have done to prepare your testimony about benzo[a]pyrene, that small repeated doses of benzo[a]pyrene are much more effective in inducing tumors than one large dose?

A. I don't know. I'm not an expert in that area.

Q. Well, let's look at the 1991 report documenting the TLV for benzo[a]pyrene, and we'll mark that as the next exhibit.

(PLF. EXH. 19, Documentation of the Threshold Limit Values and Biological Exposure Indices, Sixth Edition, 1991, was marked for identification.)

THE WITNESS: Okay. This is not a report I've seen, but it's -- I've got a sense of what it is.

BY MR. WESTBROOK:

Q. All right. As with the others, if you need more time, sir, we will certainly give it to you to look at the document.

First of all, are you familiar with what a TLV is, a threshold limit value?

A. In a general sense. We as chemists handle a lot of chemicals in the laboratory, and I think we look at a variety of information,

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particularly on MSDS sheets, as to how we should handle those chemicals.

Q. Are you aware, Doctor, that there are some substances that are considered to be so dangerous that the ACGIH has not even set a TLV for them?

A. I'm not -- you know, I'm not really familiar with those kinds of details frankly.

Q. All right. Do you know what the ACGIH is? Have you heard that term?

A. I've heard the term. I'm not sure what it is.

Q. Do you connect it with a group that sets the TLVs for various substances and reviews them?

A. I don't know.

Q. Let me ask you about something on the point we are discussing and see if we can talk about it for a minute.

On page 129 of this document as numbered, under the paragraph TLV recommendation, the committee says, quote:

The results of the epidemiologic and animal studies indicate the need for the establishment of rigorous control standards for B[a]P. Although epidemiologic data are not

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quantitative in nature, it is obvious that an increased exposure to B[a]P is hazardous.

First of all, would you disagree with the committee saying that increased exposure to B[a]P is hazardous?

MR. McDERMOTT: Object to the form of the question. No foundation. You may answer.

THE WITNESS: I don't know. I really don't.

BY MR. WESTBROOK:

Q. Okay. Going down about three lines, I want to direct your attention to the sentence that begins: Because small, repeated doses of B[a]P are more effective at tumor initiation than single administrations and because these people are probably exposed to other synergistically reacting pollutants, they are exceeding safe exposure levels.

With reference to the first part of that sentence, that small, repeated doses of B[a]P are more effective at tumor initiation than single administrations, is that something that you have a basis to agree or disagree with?

A. I can't one way or the other.

Q. All right. Would you agree with me, sir, that your chart attempting to equate 100,000

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cigarettes' worth of B[a]P to one Equal packet is an attempt to equate 100,000 smaller doses of something with one large dose?

MR. McDERMOTT: Object. Argumentative and does not summarize fairly the witness' prior testimony. He has already described the purpose of this chart.

THE WITNESS: I think I am getting frustrated because I have described the purpose of this chart in one of my earlier answers, and it was simply to help people understand that roughly what ten nanograms or a nanogram level constituent, what that is, because it's hard for people to understand, including many people, not just juries, to understand how small a nanogram or a microgram or a milligram is.

So that's the only purpose of this chart.

BY MR. WESTBROOK:

Q. So that you were not attempting in any way to say that the B[a]P from 100 million cigarettes was no more dangerous than the amount of B[a]P that you could stuff into an Equal packet? You weren't staying that?

A. In my testimony, nor in my intent for this chart, in either case, was I making -- was I

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trying to make any statement or claim relating to health. This is just simply to help people understand that nanograms are extremely low quantities.

Q. All right.

A. That's all.

Q. And do you know, sir, if there has been set a safe level for B[a]P exposure by the ACGIH?

A. I don't know.

Q. Doctor, when you said on your chart, the Equal chart, that the amount of B[a]P to fill a one-gram package of Equal was equivalent to two packs a day for more than 6,500 years, is it your testimony that you were not equating the danger of two packs a day for 6,500 years with a packet of Equal?

A. Absolutely. That was not my intent, nor was that what I said in testimony.

Q. Doctor, do you have any understanding of how many doses of a carcinogen it takes to cause cancer in a human?

A. You know, I can't even begin to answer that. I mean, again, carcinogenesis is not a fixed property of a chemical. It depends on the level and the tissue and a variety of things. I mean, I'm just not qualified to begin to answer that.

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Q. You have a listing here that a 1992 Winston contained 10 nanograms of B[a]P. Do you have any view on whether that's a safe level of B[a]P to be administered in a cigarette?

A. I have no idea. Again, all I was trying to show was that 10 nanograms is an exceedingly small quantity. There was another exhibit, a companion exhibit to this, that showed a 1954 Winston that was much higher. And the point of that was there has been a significant reduction in B[a]P in cigarette smoke over the years.

Q. Doctor, one of the other documents supplied to us by your counsel is something called a Banbury report entitled "A Safe Cigarette?".

Are you familiar with that document?

A. Yes, I am.

MR. WESTBROOK: Let's mark that as next.

(PLF. EXH. 20, Banbury Report entitled "A Safe Cigarette?", was marked for identification.)

BY MR. WESTBROOK:

Q. Doctor, since this was provided to us in your reliance materials, I assume you are familiar with this excerpt from the report?

A. Yeah, I'm familiar with it. It's been a

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DAVID E. TOWNSEND, Ph.D. - EX. BY MR. WESTBROOK

while since I reviewed this particular section. It is an excerpt of the Banbury report.

Q. All right. Were you involved in the group that prepared this Banbury report?

A. No.

Q. Okay. The report apparently was issued or concerns events that took place in 1979. Is that your recollection?

A. Yeah. The meeting, the Banbury conference, took place in 1979. I think this particular proceedings was issued in 1980.

Q. And the excerpt that was provided to us by your counsel concerns a discussion that took place apparently on Monday evening, October 15th, 1979; is that right?

A. Right.

Q. Okay. And I wanted to ask you about a couple portions of that discussion. On page 168, sir, there is a discussion in which a Dr. Bock participates. Who is Dr. Bock?

A. I don't know Dr. Bock personally. I did meet him at one point. He is -- I frankly don't know his background. I think he is a medical researcher.

Q. And how about-- and Dr. Gori is listed also. Who is Dr. Gori?

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A. Dr. Gori is a scientists who was, up until the late '70s, was NCI's director of the smoking and health program.

Q. Do you know Dr. Gori?

A. I have met Dr. Gori. I don't know him well.

Q. Have you worked with him on any committee or group?

A. No.

Q. Directing your attention to page 168, in the middle, Dr. Bock is quoted as saying, quote:

In 1955, the cigarette industry people I talked to were unanimous in saying that you could never market a cigarette delivering 15 milligrams tar. It's obvious that they can sell just about anything when they do it gradually, unquote.

From your testimony today, Doctor, is it true that RJR sells a number of cigarettes which deliver 15 milligrams of tar?

A. R. J. Reynolds sells a variety of products ranging from 15 milligrams or actually from slightly higher than that down to almost nothing. So there is a range of products.

Q. Okay. All right. So if it's true what Dr. Bock says in this document that you have provided

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to us as your reliance materials, if it's true that the industry told him in 1955 that you couldn't market a cigarette delivering 15 milligrams of tar, what the industry told Dr. Bock in 1955 turns out to be inaccurate; is that right?

A. That would be my take on it.

Q. All right. And then Dr. Gori says, quote:

Two years ago, the cigarette industry was telling me adamantly that they could not produce a cigarette with a tar-to-nicotine ratio of less than ten to one, and to date there is some on the market that go far beyond that. I believe that practically everything is possible if we give the market time to adjust to the changes that are going to be introduced.

Now, two years ago, as Dr. Gori states here, 1979, would be just about the time that you came with R. J. Reynolds, correct?

A. Yeah, that's pretty close.

Q. All right. Do you recall it being the adamant view of the industry that you could not produce a cigarette with a tar-to-nicotine ratio of less than ten to one?

A. I don't recall that as an adamant view

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expressed at R. J. Reynolds. I can't speak for the other companies. I have no idea.

Q. Does R. J. Reynolds have the capacity, sir, to adjust the tar-and-nicotine ratio in its cigarettes?

A. Let me back up. If you look at commercial products on the market today, there is a variety over -- over a certain range of tar-to-nicotine ratios. Some of the tools that are used for tar reduction so that we can market -- so we can manufacture and market ultra low or the lowest products, those tools, the design tools, in fact, will result in a somewhat different tar-to-nicotine ratio.

So in today's market, there is a current range of tar-to-nicotine ratios. All products are not the same.

Q. So is the answer to my question, yes, that the industry does have the ability to adjust tar and nicotine ratios at least within a range?

A. For consumer acceptable products, there are a range of tar-to-nicotine ratios that by and large track the tar level. It's very difficult to take one particular product, say at ten milligrams of tar, and develop a range of tar-to-nicotine ratios

and maintain consumer acceptance. Technically, it's possible. No question about it.

Maintaining consumer acceptance is the issue. Because at a certain tar level, let's take ten as an example, it turns out that there is a fairly narrow range of acceptable tar-to-nicotine ratios. If the tar-to-nicotine ratio is a bit high in that range, the acceptance falls off.

If that tar-to-nicotine ratio is low for that range, the acceptance falls off.

Q. Do you know that from commercial cigarettes that have been marketed with varying tar-to-nicotine ratios?

A. No, we know that from extensive product development and consumer testing with prototypes.

Q. You've never tried that out on the market, though, have you?

A. We've never been able to effect a significant change in tar-to-nicotine ratio, a major reduction or major change, either direction, of tar-to-nicotine ratio and maintain consumer acceptance at that specific tar level.

Q. But by maintaining consumer acceptance, do you mean that you've changed the tar and nicotine ratio and put the cigarettes out on the market to see

what happened, or are you talking about more limited testing in front of panels?

A. No, we're talking about large scale mailout consumer tests or sensory evaluations of those products. Some of those can be extended use test panels. There is a variety of tests that have been done.

Q. But they don't include an actual change in the tar-to-nicotine ratio of a commercial cigarette and then putting it out on the market in that changed form, do they?

A. No. The products we put into the market need to be consumer acceptable. So we may even get to a test market. For example, in the case -- as we did in the case of Premier. You get as far as a test market that's an extended use in a particular locale and see whether the consumers will accept it.

But, no, if your question is, have we gone in and modified existing product and dramatically changed the tar-to-nicotine ratio, the answer is no.

Q. Is it correct as a general matter that you can manufacture 1,000 cigarettes for about $9 in cost?

A. That's a fair number.

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Q. All right. So roughly 900 pennies makes 1,000 cigarettes in cost?

A. 900 pennies, okay.

Q. All right. I'm trying to get to a comparison. It's less than a penny a cigarette to manufacture?

A. You can maybe draw a chart with Equal. Sorry.

Q. I'll leave that for you, sir. So for less than a penny a cigarette, you can manufacture a cigarette in cost?

A. Okay.

Q. All right. So a cigarette pack costs about roughly 20 cents to make?

A. Roughly 9,000 -- $99 per thousand.

Q. 20 cents a pack?

A. So that's $9 for five cartons.

Q. How much a pack?

A. Uh?

Q. How much a pack?

A. Well, 25 cents or so.

Q. Okay. And cigarettes are selling on the retail market now for would you say about $1.50 to $2 depending on the market?

A. Depending on the state and the state

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taxes that are levied, sure.

Q. Okay. And we obviously have the issue of taxes.

Would you agree with me that even putting taxes aside, that cigarettes are a fairly high profit item for RJR?

A. Compared to certain other industries, cigarettes are a relatively high profit margin.

Q. All right. And it's a market in which RJR wishes to stay in this country for as long as possible?

A. Of course.

Q. All right. And despite the smoking and health issues that have come out, it's RJR's intention to continue to sell cigarettes in this country as long as it can?

A. Cigarettes -- cigarettes are a legal product in this country; and as long as they remain legal and not prohibited, we would like to do business here.

MR. WESTBROOK: Let's take a break.

MR. McDERMOTT: Are you about done?

MR. WESTBROOK: Yeah, we're real close to finishing.

MR. McDERMOTT: Okay. Do I need to

51676 0256

change my reservations is what I'm inquiring.

MR. WESTBROOK: Where is your plane, here?

MR. McDERMOTT: No, Greensboro.

THE VIDEOGRAPHER: We will go off the videotape record. The time is 4:29.

(Off-the-record conference.)

THE VIDEOGRAPHER: Back on the videotape record now. The time is 4:34.

MR. WESTBROOK: Dr. Townsend, that's all the questions I have for you today. Thank you, sir.

MR. McDERMOTT: Okay. No questions. Thank you.

THE VIDEOGRAPHER: That concludes tape 4 and the time is 4:34 PM.

(The deposition was concluded at 4:34 PM.)

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SIGNATURE OF DEPONENT

I, the undersigned, DAVID EUGENE TOWNSEND, Ph.D., do hereby certify that I have read the foregoing deposition and find it to be a true and accurate transcription of my testimony, with the following corrections, if any:

PAGE LINE CHANGE REASON

____

DAVID EUGENE TOWNSEND, Ph.D. Date

51676 0258

CERTIFICATE OF REPORTER

I, A. William Roberts, Jr., Registered Professional Reporter and Notary Public for the State of South Carolina at Large, do hereby certify:

That the foregoing deposition was taken before me on the date and at the time and location stated on page 1 of this transcript; that the witness was duly sworn to testify to the truth, the whole truth, and nothing but the truth; that the testimony of the witness and all objections made at the time of the examination were recorded stenographically by me and were thereafter transcribed by computer-aided transcription; that the foregoing deposition as typed is a true, accurate, and complete record of the testimony of the witness and of all objections made at the time of the examination.

I further certify that I am neither related to nor counsel for any party to the cause pending or interested in the events thereof.

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Witness my hand, I have hereunto affixed my official seal this 30th day of May, 1997 at Charleston, Charleston County, South Carolina.

A. William Roberts, Jr.
Registered Professional
Reporter, CP, CM
My Commission expires
May 22, 2001

I N D E X

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Westbrook

IN THE CIRCUIT COURT, FIFTEENTH JUDICIAL CIRCUIT
IN AND FOR PALM BEACH COUNTY, FLORIDA

STATE OF FLORIDA, et al, CASE NO. CL 95 1466AH

Plaintiffs,

vs.

AMERICAN TOBACCO COMPANY, et al.,

Defendants.

PLAINTIFF'S NOTICE OF VIDEO DEPOSITION DUCES TECUM

PLEASE TAKE NOTICE that pursuant to the Florida Rules of Civil Procedure, Plaintiff will take the videographic deposition of **David E. Townsend, Ph.D., Defendants' expert witness,** commencing at **9:00 a.m.** on **May 29, 1997 at Adams Mark Hotel, 425 N. Cherry Street, Winston-Salem, NC 27101.**

At least five working days prior to deposition, **David E. Townsend, Ph.D.** should produce the following documents (delivered by that date) to: **Jodi Flowers, Esquire,** + Ed Westbrook **151 Meeting Street, Suite 600, Charleston, SC 29401.**

1. Documents which counsel provided the witness that pertain to the subject matter of the witness's expected testimony.

2. Documents which the witness has specifically reviewed in preparation for his testimony in this case which relate to his testimony in this case.

3. Documents prepared by the witness in connection with his or her testimony in this case.

4. Medical/scientific articles the witness presently anticipates specifically referring to during his direct testimony (not intended to limit or restrict testimony).

5. Reports prepared specifically for this case which are not published.

6. Billing records in connection with this case.

Townsend
Exhibit Pl. 1
Date 5/29/97
A.W.R. & Assoc.

51676 0294

7. List of prior testimony in smoking and health litigation if known to witness (and if no defendant in this case was a party); a copy of transcripts if available.

The above deposition will be taken upon oral videographic examination pursuant to the Florida Rules of Civil Procedure. You are invited to attend and take part as you deem necessary and proper.

Respectfully submitted,

Ann K. Ritter/vw

ANN KIMMEL RITTER
COUNSEL FOR PLAINTIFF
NESS, MOTLEY, LOADHOLT,
RICHARDSON & POOLE
151 Meeting Street, Suite 600
Charleston, South Carolina 29401

Telephone: (803) 720-9000
Facsimile: (803) 720-9285

Dated: May 8, 1997
Charleston, South Carolina

51676 0295

CERTIFICATE OF SERVICE

I, Ann Kimmel Ritter, of the law firm of Ness, Motley, Loadholt, Richardson & Poole, P.A., do hereby certify that I have this day forwarded the above and foregoing PLAINTIFF'S NOTICE OF DEPOSITION of **David E. Townsend, Ph.D.** to the following counsel of record:

Defense Counsel:

Murray R. Garnick, Esquire Arnold & Porter 555 Twelfth Street, N.W. Washington, D.C. 20004-1202	Telephone: Facsimile:	(202) 942-5716 (202) 942-5999
Stephen J. Krigbaum, Esquire Carlton, Fields, Ward, Emmanuel, Smith & Cutler, P.A. Esperante 222 Lakeview Avenue, Ste. 1400 West Palm Beach, FL 33401	Telephone: Facsimile:	(407) 659-7070 (407) 659-7368
Edward A. Moss, Esquire Anderson, Moss, Parks & Sherouse, P.A. 25th Floor, New World Tower 100 North Biscayne Boulevard Miami, FL 33132	Telephone: Facsimile:	(305) 358-5171 (305) 358-7470
Justus Reid, Esquire Reid, Metzger & Associates, P.A. 250 Australian Avenue South, Ste. 700 West Palm Beach, FL 33401	Telephone: Facsimile:	(561) 659-7700 (561) 659-6377
Mary Percifull, Esquire Arnold & Porter Thurman Arnold Building 555 12th Street, N.W. Washington, D.C. 20004	Tel: Fax:	(202) 942-5000 (202) 942-5999

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Robert M. Montgomery, Esquire
Montgomery & Larmoyeux
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West Palm Beach, FL 33402
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Facsimile: (561) 832-0887

John Wayne Hogan, Esquire
Brown, Terrell, Hogan, Ellis, McClamma & Yogelwelm, P.A.
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Telephone: (904) 632-2424
Facsimile: (904) 632-2027

William C. Gentry, Esquire
Gentry, Phillips, Smith & Hodak, P.A.
Six East Bay Street, Suite 400
P. O. Box 837
Jacksonville, FL 32201
Telephone: (904) 356-4100
Facsimile: (904) 356-4260

Dated this 8 day of May, 1997.

Ann K Ritter/KW
ANN KIMMEL RITTER
Counsel for Plaintiff

April 30, 1997

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FLORIDA RULES OF CIVIL PROCEDURE

Effective January 1, 1967 (187 So.2d 598)

Including Amendments Effective January 1, 1997

Research Note

See West's Florida Statutes Annotated, *Volumes 30, 30A, and 31, for historical notes, comments, and judicial constructions.*

See DeFoor and Schultz, Florida Civil Procedure Forms, *for commentary and forms involving the Florida Rules of Civil Procedure.*

Use WESTLAW® *to find cases citing a rule. In addition, use* WESTLAW *to find a specific term or to update a rule; see the FL-RULES and FL-ORDERS Scope Screens for further information.*

Amendments to these rules are published, as received, in the Southern Reporter 2d *and* Florida Cases *advance sheets.*

Exhibit PL 2
Date 5/29/97
A.W.R. & Assoc.

Table of Rules

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(4) *Use of Deposition.* A deposition taken under this rule may be used in any action involving the same subject matter subsequently brought in any court in accordance with rule 1.330.

(b) Pending Appeal. If an appeal has been taken from a judgment of any court or before the taking of an appeal if the time therefor has not expired, the court in which the judgment was rendered may allow the taking of the depositions of witnesses to perpetuate their testimony for use in the event of further proceedings in the court. In such case the party who desires to perpetuate the testimony may make a motion for leave to take the deposition upon the same notice and service as if the action was pending in the court. The motion shall show (1) the names and addresses of persons to be examined and the substance of the testimony which the movant expects to elicit from each, and (2) the reason for perpetuating their testimony. If the court finds that the perpetuation of the testimony is proper to avoid a failure or delay in justice, it may make an order allowing the deposition to be taken and may make orders of the character provided for by these rules, and thereupon the deposition may be taken and used in the same manner and under the same conditions as are prescribed in these rules for depositions taken in actions pending in the court.

(c) Perpetuation by Action. This rule does not limit the power of a court to entertain an action to perpetuate testimony.

Amended Oct. 9, 1980, effective Jan. 1, 1981 (391 So.2d 165); Sept. 13, 1984, effective Jan. 1, 1985 (458 So.2d 245); July 16, 1992, effective Jan. 1, 1993 (604 So.2d 1110).

Committee Notes

1980 Amendment. Subdivision (d) is repealed because depositions de bene esse are obsolete. Rules 1.280 and 1.310 with the remainder of this rule cover all needed deposition circumstances and do so better. Subdivision (d) was taken from former chapter 63, Florida Statutes, and is not a complete procedure without reference to the parts of the statute not carried forward in the rule.

RULE 1.300 PERSONS BEFORE WHOM DEPOSITIONS MAY BE TAKEN

(a) Persons Authorized. Depositions may be taken before any notary public or judicial officer or before any officer authorized by the statutes of Florida to take acknowledgments or proof of executions of deeds or by any person appointed by the court in which the action is pending.

(b) In Foreign Countries. In a foreign country depositions may be taken (1) on notice before a person authorized to administer oaths in the place in which the examination is held, either by the law thereof or by the law of Florida or of the United States, (2) before a person commissioned by the court, and a person so commissioned shall have the power by virtue of the commission to administer any necessary oath and take testimony, or (3) pursuant to a letter rogatory. A commission or a letter rogatory shall be issued on application and notice and on terms that are just and appropriate. It is not requisite to the issuance of a commission or a letter rogatory that the taking of the deposition in any other manner is impracticable or inconvenient and both a commission and a letter rogatory may be issued in proper cases. A notice or commission may designate the person before whom the deposition is to be taken either by name or descriptive title. A letter rogatory may be addressed "To the Appropriate Authority in ______ (name of country)." Evidence obtained in response to a letter rogatory need not be excluded merely for the reason that it is not a verbatim transcript or that the testimony was not taken under oath or any similar departure from the requirements for depositions taken within Florida under these rules.

(c) Selection by Stipulation. If the parties so stipulate in writing, depositions may be taken before any person at any time or place upon any notice and in any manner and when so taken may be used like other depositions.

(d) Persons Disqualified. Unless so stipulated by the parties, no deposition shall be taken before a person who is a relative, employee, attorney, or counsel of any of the parties, is a relative or employee of any of the parties' attorney or counsel, or is financially interested in the action.

Amended July 16, 1992, effective Jan. 1, 1993 (604 So.2d 1110).

RULE 1.310 DEPOSITIONS UPON ORAL EXAMINATION

(a) When Depositions May Be Taken. After commencement of the action any party may take the testimony of any person, including a party, by deposition upon oral examination. Leave of court, granted with or without notice, must be obtained only if the plaintiff seeks to take a deposition within 30 days after service of the process and initial pleading upon any defendant, except that leave is not required (1) if a defendant has served a notice of taking deposition or otherwise sought discovery, or (2) if special notice is given as provided in subdivision (b)(2) of this rule. The attendance of witnesses may be compelled by subpoena as provided in rule 1.410. The deposition of a person confined in prison may be taken only by leave of court on such terms as the court prescribes.

(b) Notice; Method of Taking; Production at Deposition.

(1) A party desiring to take the deposition of any person upon oral examination shall give reasonable notice in writing to every other party to the action. The notice shall state the time and place for taking the deposition and the name and address of each person to be examined, if known, and, if the name is

not known, a general description sufficient to identify the person or the particular class or group to which the person belongs. If a subpoena duces tecum is to be served on the person to be examined, the designation of the materials to be produced under the subpoena shall be attached to or included in the notice.

(2) Leave of court is not required for the taking of a deposition by plaintiff if the notice states that the person to be examined is about to go out of the state and will be unavailable for examination unless a deposition is taken before expiration of the 30-day period under subdivision (a). If a party shows that when served with notice under this subdivision that party was unable through the exercise of diligence to obtain counsel to represent the party at the taking of the deposition, the deposition may not be used against that party.

(3) For cause shown the court may enlarge or shorten the time for taking the deposition.

(4) Any deposition may be recorded by videotape without leave of the court or stipulation of the parties, provided the deposition is taken in accordance with this subdivision.

(A) Notice. A party intending to videotape a deposition shall state in the notice that the deposition is to be videotaped and shall give the name and address of the operator.

(B) Stenographer. Videotaped depositions shall also be recorded stenographically, unless all parties agree otherwise.

(C) Procedure. At the beginning of the deposition, the officer before whom it is taken shall, on camera: (i) identify the style of the action, (ii) state the date, and (iii) swear the witness.

(D) Custody of Tape and Copies. The attorney for the party requesting the videotaping of the deposition shall take custody of and be responsible for the safeguarding of the videotape, shall permit the viewing of it by the opposing party, and, if requested, shall provide a copy of the videotape at the expense of the party requesting the copy.

(E) Cost of Videotaped Depositions. The party requesting the videotaping shall bear the initial cost of videotaping.

(5) The notice to a party deponent may be accompanied by a request made in compliance with rule 1.350 for the production of documents and tangible things at the taking of the deposition. The procedure of rule 1.350 shall apply to the request.

(6) In the notice a party may name as the deponent a public or private corporation, a partnership or association, or a governmental agency, and designate with reasonable particularity the matters on which examination is requested. The organization so named shall designate one or more officers, directors, or managing agents, or other persons who consent to do so, to testify on its behalf and may state the matters on which each person designated will testify. The persons so designated shall testify about matters known or reasonably available to the organization. This subdivision does not preclude taking a deposition by any other procedure authorized in these rules.

(7) On motion the court may order that the testimony at a deposition be taken by telephone. The order may prescribe the manner in which the deposition will be taken. A party may also arrange for a stenographic transcription at that party's own initial expense.

(c) Examination and Cross-Examination; Record of Examination; Oath; Objections. Examination and cross-examination of witnesses may proceed as permitted at the trial. The officer before whom the deposition is to be taken shall put the witness on oath and shall personally, or by someone acting under the officer's direction and in the officer's presence, record the testimony of the witness, except that when a deposition is being taken by telephone, the witness shall be sworn by a person present with the witness who is qualified to administer an oath in that location. The testimony shall be taken stenographically or recorded by any other means ordered in accordance with subdivision (b)(4) of this rule. If requested by one of the parties, the testimony shall be transcribed at the initial cost of the requesting party and prompt notice of the request shall be given to all other parties. All objections made at time of the examination to the qualifications of the officer taking the deposition, the manner of taking it, the evidence presented, or the conduct of any party, and any other objection to the proceedings shall be noted by the officer upon the deposition. Any objection during a deposition shall be stated concisely and in a nonargumentative and nonsuggestive manner. A party may instruct a deponent not to answer only when necessary to preserve a privilege, to enforce a limitation on evidence directed by the court, or to present a motion under subdivision (d). Otherwise, evidence objected to shall be taken subject to the objections. Instead of participating in the oral examination, parties may serve written questions in a sealed envelope on the party taking the deposition and that party shall transmit them to the officer, who shall propound them to the witness and record the answers verbatim.

(d) Motion to Terminate or Limit Examination. At any time during the taking of the deposition, on motion of a party or of the deponent and upon a showing that the examination is being conducted in bad faith or in such manner as unreasonably to annoy, embarrass, or oppress the deponent or party, or that objection and instruction to a deponent not to answer are being made in violation of rule 1.310(c), the court in which the action is pending or the circuit court where the deposition is being taken may order the officer conducting the examination to cease forthwith from taking the deposition or may limit the scope and manner of the taking of the deposition under rule 1.280(c). If the order terminates the examination, it

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shall be resumed thereafter only upon the order of the court in which the action is pending. Upon demand of any party or the deponent, the taking of the deposition shall be suspended for the time necessary to make a motion for an order. The provisions of rule 1.380(a) apply to the award of expenses incurred in relation to the motion.

(e) Witness Review. If the testimony is transcribed, the transcript shall be furnished to the witness for examination and shall be read to or by the witness unless the examination and reading are waived by the witness and by the parties. Any changes in form or substance that the witness wants to make shall be listed in writing by the officer with a statement of the reasons given by the witness for making the changes. The changes shall be attached to the transcript. It shall then be signed by the witness unless the parties waived the signing or the witness is ill, cannot be found, or refuses to sign. If the transcript is not signed by the witness within a reasonable time after it is furnished to the witness, the officer shall sign the transcript and state on the transcript the waiver, illness, absence of the witness, or refusal to sign with any reasons given therefor. The deposition may then be used as fully as though signed unless the court holds that the reasons given for the refusal to sign require rejection of the deposition wholly or partly, on motion under rule 1.330(d)(4).

(f) Filing; Exhibits.

(1) If the deposition is transcribed, the officer shall certify on each copy of the deposition that the witness was duly sworn by the officer and that the deposition is a true record of the testimony given by the witness. Documents and things produced for inspection during the examination of the witness shall be marked for identification and annexed to and returned with the deposition upon the request of a party, and may be inspected and copied by any party, except that the person producing the materials may substitute copies to be marked for identification if that person affords to all parties fair opportunity to verify the copies by comparison with the originals. If the person producing the materials requests their return, the officer shall mark them, give each party an opportunity to inspect and copy them, and return them to the person producing them and the materials may then be used in the same manner as if annexed to and returned with the deposition.

(2) Upon payment of reasonable charges therefor the officer shall furnish a copy of the deposition to any party or to the deponent.

(3) A copy of a deposition may be filed only under the following circumstances:

(A) It may be filed by a party or the witness when the contents of the deposition must be considered by the court on any matter pending before the court. Prompt notice of the filing of the deposition shall be given to all parties unless notice is waived. A party filing the deposition shall furnish a copy of the deposition or the part being filed to other parties unless the party already has a copy.

(B) If the court determines that a deposition previously taken is necessary for the decision of a matter pending before the court, the court may order that a copy be filed by any party at the initial cost of the party.

(g) Obtaining Copies. A party or witness who does not have a copy of the deposition may obtain it from the officer taking the deposition unless the court orders otherwise. If the deposition is obtained from a person other than the officer, the reasonable cost of reproducing the copies shall be paid to the person by the requesting party or witness.

(h) Failure to Attend or to Serve Subpoena; Expenses.

(1) If the party giving the notice of the taking of a deposition fails to attend and proceed therewith and another party attends in person or by attorney pursuant to the notice, the court may order the party giving the notice to pay to the other party the reasonable expenses incurred by the other party and the other party's attorney in attending, including reasonable attorney fees.

(2) If the party giving the notice of the taking of a deposition of a witness fails to serve a subpoena upon the witness and the witness because of the failure does not attend and if another party attends in person or by attorney because that other party expects the deposition of that witness to be taken, the court may order the party giving the notice to pay to the other party the reasonable expenses incurred by that other party and that other party's attorney in attending, including reasonable attorney fees.

Amended July 26, 1972, effective Jan. 1, 1973 (265 So.2d 21); Dec. 13, 1976, effective Jan. 1, 1977 (339 So.2d 626); June 14, 1979, effective July 1, 1979 (372 So.2d 449); Sept. 10, 1981, effective Jan. 1, 1982 (403 So.2d 926); Sept. 13, 1984, effective Jan. 1, 1985 (458 So.2d 245); Oct. 6 and Dec. 30, 1988, effective Jan. 1, 1989 (536 So.2d 974); July 16, 1992, effective Jan. 1, 1993 (604 So.2d 1110); Oct. 31, 1996, effective Jan. 1, 1997 (682 So.2d 105).

Committee Notes

1972 Amendment. Derived from Federal Rule of Civil Procedure 30 as amended in 1970. Subdivision (a) is derived from rule 1.280(a); subdivision (b) from rule 1.310(a) with additional matter added; the first sentence of subdivision (c) has been added and clarifying language added throughout the remainder of the rule.

1976 Amendment. Subdivision (b)(4) has been amended to allow the taking of a videotaped deposition as a matter of right. Provisions for the taxation of costs and the entry of a standard order are included as well. This new amendment allows the contemporaneous stenographic transcription of a videotaped deposition.

1988 Amendment. The amendments to subdivision (b)(4) are to provide for depositions by videotape as a matter of right.

The notice provision is to ensure that specific notice is given that the deposition will be videotaped and to disclose the identity of the operator. It was decided not to make special provision for a number of days' notice.

The requirement that a stenographer be present (who is also the person likely to be swearing the deponent) is to ensure the availability of a transcript (although not required). The transcript would be a tool to ensure the accuracy of the videotape and thus eliminate the need to establish other procedures aimed at the same objective (like time clocks in the picture and the like). This does not mean that a transcript must be made. As at ordinary depositions, this would be up to the litigants.

Technical videotaping procedures were not included. It is anticipated that technical problems may be addressed by the court on motions to quash or motions for protective orders.

Subdivision (c) has been amended to accommodate the taking of depositions by telephone. The amendment requires the deponent to be sworn by a person authorized to administer oaths in the deponent's location and who is present with the deponent.

1992 Amendment. Subdivision (b)(4)(D) is amended to clarify an ambiguity in whether the cost of the videotape copy is to be borne by the party requesting the videotaping or by the party requesting the copy. The amendment requires the party requesting the copy to bear the cost of the copy.

1996 Amendment. Subdivision (c) is amended to state the existing law, which authorizes attorneys to instruct deponents not to answer questions only in specific situations. This amendment is derived from Federal Rule of Civil Procedure 30(d) as amended in 1993.

Court Commentary

1984 Amendment. Subdivision (b)(7) is added to authorize deposition by telephone, with provision for any party to have a stenographic transcription at that party's own initial expense.

Subdivision (d) is changed to permit any party to terminate the deposition, not just the objecting party.

Subdivision (e) is changed to eliminate the confusing requirement that a transcript be submitted to the witness. The term has been construed as requiring the court reporter to travel, if necessary, to the witness, and creates a problem when a witness is deposed in Florida and thereafter leaves the state before signing. The change is intended to permit the parties and the court reporter to handle such situations on an ad hoc basis as is most appropriate.

Subdivision (f) is the committee's action in response to the petition seeking amendment to rule 1.310(f) filed in the Supreme Court Case No. 62,699. Subdivision (f) is changed to clarify the need for furnishing copies when a deposition, or part of it, is properly filed, to authorize the court to require a deposition to be both transcribed and filed, and to specify that a party who does not obtain a copy of the deposition may get it from the court reporter unless ordered otherwise by the court. This eliminates the present requirement of furnishing a copy of the deposition, or material part of it, to a person who already has a copy in subdivision (f)(3)(A).

Subdivision (f)(3)(B) broadens the authority of the court to require the filing of a deposition that has been taken, but not transcribed.

Subdivision (g) requires a party to obtain a copy of the deposition from the court reporter unless the court orders otherwise. Generally, the court should not order a party who has a copy of the deposition to furnish it to someone who has neglected to obtain it when the deposition was transcribed. The person should obtain it from the court reporter unless there is a good reason why it cannot be obtained from the reporter.

RULE 1.320 DEPOSITIONS UPON WRITTEN QUESTIONS

(a) Serving Questions; Notice. After commencement of the action any party may take the testimony of any person, including a party, by deposition upon written questions. The attendance of witnesses may be compelled by the use of subpoena as provided in rule 1.410. The deposition of a person confined in prison may be taken only by leave of court on such terms as the court prescribes. A party desiring to take a deposition upon written questions shall serve them with a notice stating (1) the name and address of the person who is to answer them, if known, and, if the name is not known, a general description sufficient to identify the person or the particular class or group to which that person belongs, and (2) the name or descriptive title and address of the officer before whom the deposition is to be taken. A deposition upon written questions may be taken of a public or private corporation, a partnership or association, or a governmental agency in accordance with rule 1.310(b)(6). Within 30 days after the notice and written questions are served, a party may serve cross questions upon all other parties. Within 10 days after being served with cross questions, a party may serve redirect questions upon all other parties. Within 10 days after being served with redirect questions, a party may serve recross questions upon all other parties. The court may for cause shown enlarge or shorten the time.

(b) Officer to Take Responses and Prepare Record. A copy of the notice and copies of all questions served shall be delivered by the party taking the depositions to the officer designated in the notice, who shall proceed promptly to take the testimony of the witness in the manner provided by rules 1.310(c), (e), and (f) in response to the questions and to prepare the deposition, attaching the copy of the notice and the questions received by the officer. The questions shall not be filed separately from the deposition unless a party seeks to have the court consider the questions before the questions are submitted to the witness.

Amended July 26, 1972, effective Jan. 1, 1973 (265 So.2d 21); Sept. 10, 1981, effective Jan. 1. 1982 (403 So.2d 926); July 16, 1992, effective Jan. 1, 1993 (604 So.2d 1110).

Committee Notes

1972 Amendment. Derived from Federal Rule of Civil Procedure 31 as amended in 1970. The name of interrogatories has been changed to questions to avoid confusion with interrogatories to parties under rule 1.340. Language

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RULE 26 EXPERT STATEMENT

David E. Townsend, Ph.D.
R.J. Reynolds Tobacco Company
Bowman Gray Technical Center
P.O. Box 1487
Winston-Salem, North Carolina 27102-1487

Subject Matter And Anticipated Testimony

Dr. Townsend will testify concerning cigarette design. He will critique the evidence and opinions presented by plaintiff on this subject. It is currently anticipated that Dr. Townsend will testify that, in the design of cigarettes, R.J. Reynolds Tobacco Company specifically, and the manufacturers of cigarettes generally, have responded both to the scientific criticisms of cigarettes and the demands of smokers. It is further anticipated that Dr. Townsend will testify that the tobacco industry as a whole and R.J. Reynolds Tobacco Company in particular have been instrumental in developing new cigarette designs that were both responsive to the various criticisms of the scientific and medical community as well as to the demands of smokers. Indeed, the tobacco industry, including R.J. Reynolds Tobacco Company, were leaders in inventing or developing such cigarette designs.

In addition, Dr. Townsend may be asked to comment upon the opinions expressed by other witnesses, as well as the evidence they rely upon, to the extent that these opinions relate to his areas of expertise.

Townsend
Exhibit Pl 3
Date 5/29/97
A.W.R. & Assoc.

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Summary Of Grounds

Dr. Townsend's expected testimony and opinions are based on:

1. His education, training and experience, as reflected on his attached c.v.

2. His review of scientific information and literature concerning the subject matter described above that are reasonably relied upon by members of his profession.

3. His review of documents from R.J. Reynolds Tobacco Company concerning the subject matter described above and, as appropriate, documents either produced by other defendants in this lawsuit concerning cigarette design or relied upon by plaintiff's experts on these subjects.

4. His review of the evidence and testimony in the case.

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DAVID E. TOWNSEND

ADDRESS:

Residence: PERSONAL/CONFIDENTIAL MATERIAL REDACTED

Office: R. J. Reynolds Tobacco Company
Bowman Gray Technical Center
P.O. Box 1487
Winston-Salem, NC 27102-1487
(910) 741-4965

BIRTH: Kansas City, Missouri
August 14, 1947

PROFESSIONAL EXPERIENCE:

July 1996 - Present — Director, Product Development, R. J. Reynolds Tobacco Company, Winston-Salem, North Carolina. Responsible for Product Development, Analytical Chemistry Research, and Analytical Chemistry Support.

June 1995 - June 1996 — Senior Principal Scientist, R. J. Reynolds Tobacco Company, Winston-Salem, North Carolina. Supervise New Product Development.

August 1992 - June 1995 — Principal Scientist, R. J. Reynolds Tobacco Company, Winston-Salem, North Carolina. Supervise New Product Development.

April 1991 - August 1992 — Principal Scientist, R. J. Reynolds Tobacco Company, Winston-Salem, North Carolina. Supervise research in the area of materials development for cigarette products.

August 1987 - March 1991 — Principal Scientist, R. J. Reynolds Tobacco Company, Winston-Salem, North Carolina. Responsible for conducting and supervising research in the areas of smoke formation, cigarette design and performance, materials development for advanced technology products, and new product development.

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DAVID E. TOWNSEND
(Continued)

February 1987 - August 1987	Principal Scientist, R. J. Reynolds Tobacco Company, Winston-Salem, North Carolina. Conducted and supervised research in the area of smoke formation and cigarette design.
January 1984 - January 1987	Master Scientist, R. J. Reynolds Tobacco Company, Winston-Salem, North Carolina. Responsible for conducting and supervising research in the areas of filtration, air dilution, cigarette design, smoke formation, and smoke physical properties and dynamics.
January 1981 - January 1984	R&D Program Manager, R. J. Reynolds Tobacco Company, Winston-Salem, North Carolina. Conducted and supervised research on smoke formation, aerosol properties, and cigarette design.
October 1977 - January 1981	Senior R&D Chemist, R. J. Reynolds Tobacco Company, Winston-Salem, North Carolina. Responsible for conducting and supervising research in the areas of filtration (including selective filtration), air dilution, the effects of cigarette construction parameters on cigarette performance, smoke physical properties, and cigarette paper R&D.
October 1974 - October 1977	R&D Chemist, Rohm & Haas Company, Philadelphia, Pennsylvania. Conducted research on low and high volume (750 mm lbs/year) acrylate and methacrylate monomer processes. Research included kinetics of homogeneous catalyzed reactions, synthesis and characterization of heterogeneous catalysts and high volume process optimization.
May 1969 - September 1969	Liggett & Myers, Durham, North Carolina. Laboratory Assistant - Primarily in the area of gas-phase deliveries of cigarettes.

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DAVID E. TOWNSEND
(Continued)

EDUCATION:

Ph.D., Physical Organic Chemistry Florida State University Tallahassee, Florida	1972-1974
M.S., Physical Organic Chemistry Florida State University Tallahassee, Florida	1969-1972
B.S., Chemistry University of North Carolina at Chapel Hill Chapel Hill, North Carolina	1965-1969

MILITARY SERVICE:

United States Army Southeastern Signal School Active Duty for Training, U.S. Army Reserve	February 1973 - June 1973

RESEARCH PUBLICATIONS:

1. The Quantum Chain Process in the Sensitized Cis-Trans Photoisomerization of 1,3-Dienes. J. AM. CHEM. SOC., 95: 5966 (1973).
2. Chemical and Physical Evidence for Anthracene-1,3-Diene Exciplexes. A Quencher sensitized Photodimerization. J. AM. CHEM. SOC., 95: 6140 (1973).
3. Mechanistic Aspects of the Sensitized Cis-Trans Photo-isomerization of 1,3-Dienes. "Symposium on Photochemistry of Hydrocarbons," Division of Petroleum Chemistry Abstracts. American Chemical Society, 1973, pp. 277-285.

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DAVID E. TOWNSEND
(Continued)

RESEARCH PUBLICATIONS:
(Continued)

4. Exciplex and Triplex Emission in the System 9,10-Dichloro-anthracene-2,5-Dimethyl-2,4-Hexadiene. J. AM. CHEM. SOC., 97: 5688 (1975).

5. The Fluorescence Spectrum and Lifetime of the Anthracene/trans,trans-2,4-Hexadiene Exciplex. CHEM. PHYS. LETT., 43, (2), 295 (1976).

6. Concerning the Participation of the Anthracene/N,N-Dimethylaniline Exciplex in Anthracene Photodimerization. J. AM. CHEM. SOC., 99(3): 884 (1977).

7. Indirect Detection of a Reversibly Formed Nonfluorescing Exciplex between Benzanthracene and cis-1,3-Pentadiene. A General Method for Treating Photochemical Data. J. AM. CHEM. SOC., 99(18): 5992 (1977).

8. A Triplet State Pathway for Adduct Formation Between Benz(a)anthracene and the 1,3-Pentadienes. J. CHEM. SOC. CHEM. COMM., 1978, p. 588.

9. Participation of the Anthracene/trans,trans-2,4-Hexadiene Exciplex in Anthracene Photodimerization. "Symposium on Organic Photochemistry," Division of Petroleum Chemistry Abstracts, Am. Chem. Soc., 1979, p. 286.

10. The Effects of Cigarette Paper Permeability and Air Dilution on Carbon Monoxide Production and Diffusion from the Tobacco Rod. Presented at 36th Tobacco Chemists' Research Conference, Raleigh, NC, 1982, and at CORESTA 1982 Symposium, Winston-Salem, NC.

11. The Effect of Tobacco Moisture on the Removal of Cigarette Smoke by the Tobacco Rod. Presented at the 37th Tobacco Chemists' Research Conference, Arlington, VA, 1983, and at CORESTA 1983 Symposium, Florence.

12. Role of Higher Triplet States in the Anthracene-Sensitized Photoisomerization of Stilbene and 2,4-Hexadiene. J. AM. CHEM. SOC., 105(9): 2530 (1983).

13. Photocycloaddition of Anthracene to trans,trans-2,4-Hexadiene. J. AM. CHEM. SOC., 108(10): 2674 (1986).

14. Processes Occurring in a Burning Cigarette. Invited Paper, HORIZONS Lecture Series, Kimberly-Clark Corporation, Atlanta, 1986.

15. Segmented Cigarette, U.S. 4,595,024, June 17, 1986.

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DAVID E. TOWNSEND
(Continued)

RESEARCH PUBLICATIONS:
(Continued)

16. Segmented Cigarette, U.S. 4,700,726, October 20, 1987.

17. Segmented Cigarettes with Uniform Burn Rates, U.S. 4,730,628, March 15, 1988.

18. A Comparative Ignition Propensity Study of Foreign and U.S. Cigarettes. J. Fire Sci., 8: 239-253 (1990).

19. The Effects of Cigarette Circumference on Ignition Propensity. J. Fire Sci., 11: 52-65 (1993).

20. A Comparative Ignition Propensity Study of Foreign and U.S. Cigarettes Using the NIST Cotton Duck Mockup Ignition Test Method. J. Fire Sci., 13: 386-398 (1995).

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UPI 04/13 1632 Cigarette industry releases list of 600 ingredients

WASHINGTON, April 13 (UPI) -- The six major U.S. tobacco companies released Wednesday the list of 600 ingredients they add in manufacturing cigarettes in a move to combat pressure for more regulation of their industry.

R.J. Reynolds Tobacco Co. revealed the ingredients on behalf of the major U.S. cigarette manufacturers, including the American Tobacco Co., Brown and Williamson, Liggett Group, Inc., Lorillard, Inc., and Philip Morris Inc.

Reynolds spokesman David Fishel said, "More than 98 percent of the ingredients are approved as food additives by the U.S. Food and Drug Administration, and have been given the status 'Generally Recognized as Safe in foods" by the FDA or other expert committees."

Critics, however, said some of the ingredients were toxic, and Rep. Ron Wyden, D-Ore., said about 100 ingredients were missing from the list that had been formerly disclosed to federal authorities.

Philip Morris spokesman Tony Andrade said, "The 600 ingredients is the complete list given to the federal government under the Federal Cigarette Labeling Act. There might be a few other ingredients added to the paper because the law does not refer to ingredients added to cigarette paper."

Congressional hearings are scheduled for Thursday to further investigate the cigarette industry.

Andrade said the ingredients list was not released in anticipation of congressional hearings, but he expected discussion of the ingredients to be on the agenda.

Among the primary ingredients, in addition to tobacco, are water, sugar, glycerin, licorice, cocoa and additional flavorings. The list of 600 ingredients, agents and chemicals that are added to the primary items during manufacture run the alphabet from acetanisole to yeast.

Some of the additives include alfalfa, ammonia, ascorbic acid, basil and bay leaf oil, caffeine, carbon dioxide, beta-carotene, ethyl alcohol, ethyl propionate, honey, smoke flavor, snakeroot oil, vanilla, wild cherry bark, wine and xanthan gum.

Cigarettes are 90 percent tobacco, Reynolds said. Other primary ingredients of 99 percent of U.S. non-menthol cigarettes also contain water, sugars, glycerin, propylene glycol, licorice, cocoa and additional flavors. Additional ingredients, the company said, for flavoring make up about 0.02 percent of cigarettes.

The Action on Smoking and Health, however, said some of the chemicals are so toxic that they could not be dumped in a landfill under federal environmental laws.

John Banzhaf, director of the anti-smoking organization, said, "It is unconscionable that the industry would be able to add chemicals too dangerous to be used in foods or even added to landfills with any governmental testing."

Banzhaf also said the ingredient list includes at least 13 chemicals "which are banned by the FDA because they are too dangerous to be allowed in foods."

The anti-smoking organization cited ethyl-2-furoate, which causes liver damage in testing on animals; freon-11, a cholorofluorocarbon; and methoprene, a pesticide used to kill insects on stored tobacco.

Pressure has been mounting recently for the tobacco industry to be more forthcoming in information on the manufacture of cigarettes. Testimony

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during March hearings chaired by Rep. Henry Waxman, D-Calif., for the Energy and Commerce Committee's subcommittee on health and the environment, suggested tobacco companies hid information about cigarette ingredients and knew that nicotine is addictive. Waxman has suggested further regulation of cigarette manufacturing.

Waxman said he also is considering legislation that would authorize the Food and Drug Administration, which currently has virtually no oversight power over the tobacco industry, to regulate cigarettes as a drug delivery system.

Waxman said he would hold a hearing of his subcommittee Thursday to investigate such matters and had sent "formal letters of invitation" to the chief executive officers and scientific research directors of Philip Morris and several other tobacco companies.

Philip Morris earlier said they were releasing the list of ingredients to show they are not harmful to smokers.

"The industry's decision to make this proprietary information publicly available to our consumers is in response to misleading allegations recently made about the nature of the ingredients used in our products," said Steven Parrish, general counsel for Philip Morris U.S.A.

Parrish said that Philip Morris and the other five companies had been submitting a list of ingredients added to tobacco used in cigarettes manufactured and sold in the United States to the Secretary of the Department of Health and Human Services (HHS) as required by the Federal Cigarette Labeling and Advertising Act each year since 1986.

The Act recognizes that cigarette ingredients are trade secrets and requires that HHS maintain strict confidentiality.

Parrish said the ingredients added to tobacco used in cigarettes manufactured and sold in the United States by Philip Morris are common foods or food additives, and are included on the Food and Drug Administration's lists of approved food additives on substances "generally recognized as safe" (GRAS), are on the Flavor Extract Manufacturers Association's GRAS list, or have been approved by federal agencies such as the Bureau of Tobacco, Alcohol and Firearms or the Environmental Protection Agency.

"Unfortunately," Parrish said, "the confidentiality that Congress mandated for cigarette ingredients information has been mischaracterized as an attempt by cigarette manufacturers to be 'secretive' and keep information from the American public."

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Box 995

PMI: State of MN

Box 995

April 12, 1994

Ingredients Added to Tobacco in the Manufacture of Cigarettes
by the Six Major American Cigarette Companies *

1. ACETANISOLE - FDA approved food additive; FEMA GRAS; found in beef, cranberry, guava, grape, mango, peppermint; used in frozen dairy products, hard candies.

2. ACETIC ACID - FDA GRAS; FEMA GRAS; found in banana, beer, beef, apple juice, apricot, blue cheese, blueberries; used in condiment relishes.

3. ACETOIN - FDA GRAS; FEMA GRAS; found in apples, butter, yogurt, asparagus, black currants, blackberry, wheat, broccoli, brussel sprouts, cantaloupe; used in baked goods.

4. ACETOPHENONE - FDA approved food additive; FEMA GRAS; found in apple, cheese, apricot, banana, beef, cauliflower; used in chewing gum.

5. 6-ACETOXYDIHYDROTHEASPIRANE - FEMA GRAS; used in baked goods, instant coffee/tea, snacks, soups, seasonings, meat products.

6. 2-ACETYL-3-ETHYLPYRAZINE - FEMA GRAS; found in pork; used in soups.

7. 2-ACETYL-5-METHYLFURAN - FEMA GRAS; found in coffee, roasted filbert, tomato juice; used in soups, nut products, snack foods, gravies.

8. ACETYLPYRAZINE - FEMA GRAS; found in beef, coffee, popcorn, sesame seed, almond, wheat bread, cocoa, peanut, pork, potato chips; used in frozen dairy products.

9. 2-ACETYLPYRIDINE - FEMA GRAS; found in cocoa, coffee, roasted peanut, potato chips, tea, beer, wheat bread, hazelnut, lamb/mutton, potato; used in breakfast cereals, ice cream, candy.

CONFIDENTIAL MATERIAL PROTECTED BY ORDER OF THE CHANCERY COURT, JACKSON COUNTY, MS, IN RE TOBACCO LITIGATION, CAUSE NO. 94-1429

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*/ The six companies are the American Tobacco Company, Brown and Williamson, Liggett Group, Inc., Lorillard, Inc., Philip Morris Incorporated and R.J. Reynolds Tobacco Company.

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10. 3-ACETYLPYRIDINE - FEMA GRAS, found in roasted filbert, cocoa; used in non-alcoholic beverages, ice cream, candy, gelatin and puddings, baked goods.

11. 2-ACETYLTHIAZOLE - FEMA GRAS, found in bean, potatoes, artichoke, asparagus, beef, beer, brazil nuts, rice, boiled shrimp, used in snack foods.

12. ACONITIC ACID - FDA GRAS; FEMA GRAS, found in beet root, sugarcane; used in alcoholic beverages, baked goods, chewing gum.

13. dl-ALANINE - FDA approved food additive, natural constituent of protein in plants and animals; found in apple, beef, carob, pea, soybean, wine, zucchini.

14. ALFALFA EXTRACT - FDA GRAS, FEMA GRAS; found in alfalfa; used in baked goods.

15. ALLSPICE EXTRACT, OLEORESIN, AND OIL - FDA GRAS; FEMA GRAS; used in soups, candies, chewing gum, meats

16. ALLYL HEXANOATE - FDA approved food additive; FEMA GRAS; found in baked potato; used in gelatin and puddings

17. ALLYL IONONE - FDA approved food additive; FEMA GRAS; used in ice cream, baked goods, candy, gelatin and puddings, jellies.

18. ALMOND BITTER OIL - FDA GRAS, FEMA GRAS; found in almond, apricot, peach kernel; used in baked goods, candy, gelatin and puddings, chewing gum.

19. AMBERGRIS TINCTURE - FDA GRAS, FEMA GRAS; used in non-alcoholic beverages, ice cream, candy.

20. AMMONIA - Occurs in human/animal breath due to protein metabolism; dissolved in water it is a naturally occurring substance that plays a vital role in protein metabolism in animals, including man.

21. AMMONIUM BICARBONATE - FDA GRAS; used in baked goods.

22. AMMONIUM HYDROXIDE - FDA GRAS; found in cured pork.

23. AMMONIUM PHOSPHATE DIBASIC - FDA GRAS; used in dough, ice cream, gelatin and puddings.

24. AMMONIUM SULFIDE - FEMA GRAS; used in baked goods, meat products, gravies, condiments.

25. AMYL ALCOHOL - FDA approved food additive; FEMA GRAS; found in apple, banana, cheese, chicken, coffee, potato, raspberry, strawberry, tomato; used in baked goods, candy, gelatin and puddings, chewing gum.

26. AMYL BUTYRATE - FDA approved food additive; FEMA GRAS; found in bananas, beer, apple juice, apricots, strawberries, wine; used in syrup, candy, chewing gum.

27. AMYL FORMATE - FDA approved food additive; FEMA GRAS; found in apples, strawberry, brandy, honey, tomatoes, whiskey; used in non-alcoholic beverages, candy, chewing gum.

28. AMYL OCTANOATE - FDA approved food additive; FEMA GRAS; found in strawberry, apple, cognac; used in baked goods, candy, gelatin and puddings.

29. alpha-AMYLCINNAMALDEHYDE - FDA approved food additive; FEMA GRAS; found in black tea, olibanum; used in candy, baked goods, chewing gum.

30. AMYRIS OIL - FDA approved food additive; found in brandies, liqueurs, amryis balsamifera; used in brandies, liqueurs, oriental specialties.

31. trans-ANETHOLE - FDA GRAS; FEMA GRAS; found in cheese, tea, apple, licorice; used in alcoholic beverages.

32. ANGELICA ROOT EXTRACT, OIL AND SEED OIL - FDA GRAS; FEMA GRAS; used in non-alcoholic beverages, alcoholic beverages, baked goods, chewing gum.

33. ANISE, ANISE STAR, EXTRACT AND OILS - FDA GRAS; FEMA GRAS; found in star anise; used in ice cream, ices, baked goods, candy, chewing gum, meats, condiments.

34. ANISYL ACETATE - FDA approved food additive; FEMA GRAS; found in currant; used in baked goods, candy, gelatin and puddings, chewing gum.

35. ANISYL ALCOHOL - FDA approved food additive; FEMA GRAS; found in honey, tomato; used in gelatin and puddings.

36. ANISYL FORMATE - FDA approved food additive; FEMA GRAS; found in vanilla; used in candy, baked goods.

37. ANISYL PHENYLACETATE - FDA approved food additive; FEMA GRAS; found in honey; used in baked goods.

38. APPLE JUICE CONCENTRATE, EXTRACT, AND SKINS - common food item found in apple; used in juices, baked goods.

39. APRICOT EXTRACT AND JUICE CONCENTRATE - Common food item found in apricot; used in condiments.

40. l-ARGININE - FDA approved food additive, natural constituent of proteins in plants and animals.

41. ASAFETIDA FLUID EXTRACT AND OIL - FDA GRAS; FEMA GRAS; used in condiments, candy, soups, meats

42. ASCORBIC ACID - FDA GRAS, FEMA GRAS; found in citrus fruit, tea leaves; used in baked goods, sweet sauce, soups, candy, gelatin and puddings, dairy products.

43. l-ASPARAGINE MONOHYDRATE - FDA approved food additive; found in proteins, licorice.

44. l-ASPARTIC ACID - FDA approved food additive; FEMA GRAS; found in proteins, licorice; used in seasonings

45. BALSAM PERU AND OIL - FDA GRAS, FEMA GRAS; found in Peru balsam; used in baked goods, syrups, candy, chewing gum.

46. BASIL OIL - FDA GRAS; FEMA GRAS; found in basil used in baked goods, condiments, meats.

47. BAY LEAF, OIL AND SWEET OIL - FDA GRAS; FEMA GRAS; found in bay leaves; used in condiments, meat

48. BEESWAX WHITE - FDA GRAS, FEMA GRAS; used in baked goods, candy, honey.

49. BEET JUICE CONCENTRATE - Beets are included among "Miscellaneous Vegetables" in FDA Standards of Identity and are also covered by a USDA Standards for Grades.

50. BENZALDEHYDE - FDA GRAS; FEMA GRAS; found in apple juice, almond, apricot, artichoke, asparagus, beans, beef, beer; used in baked goods, chewing gum.

51. BENZALDEHYDE GLYCERYL ACETAL - FDA approved food additive; FEMA GRAS; used in baked goods, candy, gelatin and puddings, chewing gum.

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52. BENZOIC ACID - FDA GRAS; FEMA GRAS; found in cinnamon, strawberry, tea, apple, beer, bread, cocoa, honey; used in baked goods, cheese, candy, chewing gum, condiment relish.

53. BENZOIN - FDA approved food additive; FEMA GRAS; used in non-alcoholic beverages, alcoholic beverages, baked goods, candy, chewing gum.

54. BENZOIN RESIN - FDA approved food additive; FEMA GRAS; used in baked goods, gelatin and puddings, chewing gum.

55. BENZOPHENONE - FDA approved food additive; FEMA GRAS; found in grape, apples, papaya; used in frozen dairy products.

56. BENZYL ALCOHOL - FDA approved food additive; FEMA GRAS; found in apricot, beef, beer, almonds, apple, apple juice, asparagus, bananas, black currants, blackberries; used in chewing gum, candy, baked goods.

57. BENZYL BENZOATE - FDA approved food additive; FEMA GRAS; found in celery, parsley, black currants, butter, guava, pineapple, papaya; used in ice cream, baked goods, candy.

58. BENZYL BUTYRATE - FDA approved food additive; FEMA GRAS; found in apple, apple juice, apricot, banana, parmesan cheese, grape, honey, mango, melon, muskmelon, orange juice, papaya; used in candy.

59. BENZYL CINNAMATE - FDA approved food additive; FEMA GRAS; used in non-alcoholic beverages, baked goods, candy.

60. BENZYL PROPIONATE - FDA approved food additive; FEMA GRAS; found in strawberry; used in candy.

61. BENZYL SALICYLATE - FDA approved food additive; FEMA GRAS; found in cranberry, apple flowers; used in baked goods.

62. BERGAMOT OIL - FDA GRAS; FEMA GRAS; found in oranges; used in icings, gelatin, alcoholic beverages.

63. BISABOLENE - FEMA GRAS; found in carrot, ginger, hops, guava, mango, ginger; used in baked goods, candy.

64. BLACK CURRANT BUDS ABSOLUTE - FDA approved food additive; FEMA GRAS; used in non-alcoholic beverages, baked goods, candy, gelatin and puddings.

65. BORNEOL - FDA approved food additiv ; FEMA GRAS; found in

carrot, blackberries, brandy, grapes, cocoa; used in baked goods.

66. BORNYL ACETATE - FDA approved food additive; FEMA GRAS; found in carrot, black currants, gin, ginger, kiwi fruit, pistacia, plum, sweet potato, soy sauce, black and green tea; used in gelatin and puddings, candy, ice cream.

67. BUCHU LEAF OIL - FDA approved food additive; FEMA GRAS; used in ice cream, ices, candy, condiments.

68. 1,3-BUTANEDIOL - FDA approved food additive; used as solvent for natural and synthetic flavors.

69. 2,3-BUTANEDIONE - FDA GRAS; FEMA GRAS; found in apple, bean, beef, butter, artichoke, avocado, black currents, blueberry, blue cheese, grape brandy, wheat, brussels sprouts; used in meat products.

70. 1-BUTANOL - FDA approved food additive; FEMA GRAS; found in apple juice, banana, beef, celery, cheese (cheddar and Swiss), peach, potato; used in non-alcoholic beverages, alcoholic beverages, ice cream, ices, candy, cream, baked goods.

71. 2-BUTANONE - FDA approved food additive; FEMA GRAS; found in apple, apricot, banana, cauliflower, celery, chicken, coffee, milk, onion, tomato; used in non-alcoholic beverages, ice cream ices, candy, baked goods.

72. 4(2-BUTENYLIDENE)-3,5,5-TRIMETHYL-2-CYCLOHEXEN-1-ONE -found in white-flesh nectarine, starfruit, grapefruit juice.

73. BUTTER, BUTTER ESTERS, AND BUTTER OIL - FDA approved food additive; FEMA GRAS; found in butter; used in frozen dairy products.

74. BUTYL ACETATE - FDA approved food additive; FEMA GRAS; found in apple, banana, beer, black currant, cashew nuts, cheese, raspberry, apricot, blackberry, brandy, cantaloupe; used in cheeses, baked goods, candy.

75. BUTYL BUTYRATE - FDA approved food additive; FEMA GRAS; found in banana, apricot, blackberry, brandy, parmesan cheese, honey, mango, melon, muskmelon, orange juice, papaya; used in candy.

76. BUTYL BUTYRYL LACTATE - FDA approved food additive; FEMA GRAS; used in non-alcoholic beverages, baked goods, candy, sweet sauces.

77. BUTYL ISOVALERATE - FDA approved food additive; FEMA GRAS; found in apple, apricot, banana, parmesan cheese, olives, pear, plum, strawberry, wine; used in baked goods.

78. BUTYL PHENYLACETATE - FDA approved food additive; FEMA GRAS; found in papaya, alfalfa; used in baked goods, ice cream, candy.

79. BUTYL UNDECYLENATE - FDA approved food additive; FEMA GRAS; no limitation for use in food other than good manufacturing practices.

80. 3-BUTYLIDENEPHTHALIDE - FEMA GRAS; found in celery, celery stalk; used in soups, condiments, meats.

81. BUTYRIC ACID - FDA GRAS, FEMA GRAS, found in apple, beef, beer, black currants, blueberries, wheat bread, butter, blue cheese; used in snack foods, candy, margarine.

82. CADINENE - FDA approved food additive, found in grapefruit, orange juice, peach, pepper, peppermint, tea; used in baked goods, candy, gelatin and puddings, meat products.

83. CAFFEINE - FDA GRAS; FEMA GRAS, found in coffee, tea, mate, kola nut; used in non-alcoholic beverages, ice cream ices, baked goods, candy, gelatin and puddings.

84. CALCIUM CARBONATE - FDA GRAS, no limitation for use in food other than good manufacturing practices Used as a dietary supplement; also used in baked goods, chewing gum, beverages

85. CAMPHENE - FDA approved food additive; FEMA GRAS; found in carrot, cheddar cheese, ginger, apricot, black currants, blackberry, celery, gin, kiwi fruit; used in candy, baked goods, ice cream

86. CANANGA OIL - FDA GRAS, FEMA GRAS; used in non-alcoholic beverages, candy, baked goods.

87. CAPSICUM OLEORESIN - found in pepper; used in non-alcoholic beverages, baked goods, condiments, candy, chewing gum, meats.

88. CARAMEL COLOR - FDA GRAS; FEMA GRAS; found in sugars; used in gravies, meats, condiments.

89. CARAWAY OIL - FDA GRAS; FEMA GRAS; found in caraway seeds; used in baked goods, condiments.

90. CARBON DIOXIDE - FDA GRAS; used in beverages, meat products, processed fruits, dairy products.

91. CARDAMOM OLEORESIN, EXTRACT, SEED OIL, AND POWDER -FDA GRAS; FEMA GRAS; found in cardamom; used in baked goods, pickles, meats.

92. CAROB BEAN AND EXTRACT - FDA GRAS; FEMA GRAS; found in carob beans; used in baked goods, candy, gelatin and puddings, icings and toppings.

93. beta-CAROTENE - FDA GRAS: found in carrot, pumpkin, spinach, broccoli, used in processed fruit and fruit juices, dairy products.

94. CARROT OIL - FDA GRAS; FEMA GRAS; found in carrots; used in baked goods.

95. CARVACROL - FDA approved food additive; FEMA GRAS; found in pepper, spearmint, tea; used in baked goods, condiments, candy, gelatin and puddings, chewing gum.

96. 4-CARVOMENTHENOL - FDA approved food additive; FEMA GRAS; found in carrot, celery seed, cocoa powder, grape, grapefruit, orange, tea, wine; used in non-alcoholic beverages, candy, baked goods, gelatin and puddings, chewing gum.

97. l-CARVONE - FDA GRAS; FEMA GRAS; found in grapefruit juice, honey, hops oil, orange juice, beer, cherries, endive, guava, hazelnuts; used in candy, condiments, baked goods.

98. beta-CARYOPHYLLENE - FDA approved food additive; FEMA GRAS; found in carrot, artichoke, banana, cashews, apples, celery, chervil, chicken, cocoa; used in chewing gum, ice cream, beverages.

99. beta-CARYOPHYLLENE OXIDE - FDA approved food additive; found in rosemary; used in beverages, ice cream, candy, condiments.

100. CASCARILLA OIL AND BARK EXTRACT - FDA GRAS; FEMA GRAS; used in baked goods, candy, condiments.

101. CASSIA BARK OIL - FDA GRAS; FEMA GRAS; found in cassia; used in meat products.

102. CASSIE ABSOLUTE AND OIL - FDA approved food additive; FEMA GRAS; found in cassie; used in candy, baked goods, ice cream.

103. CASTOREUM EXTRACT, TINCTURE AND ABSOLUTE - FDA GRAS; FEMA GRAS; found in castor; used in baked goods, condiments, candy, chewing gum.

104. CEDAR LEAF OIL - FDA approved food additive; FEMA GRAS; found in Cedar tree; used in alcoholic beverages, meats, candy.

105. CEDARWOOD OIL TERPENES AND VIRGINIANA - FDA approved food additive; found in cedarwood, clary sage oil.

106. CEDROL - FDA approved food additive, found in Cypress wood, cedar wood; used in alcoholic beverages, meat products

107. CELERY SEED EXTRACT, SOLID, OIL, AND OLEORESIN - FDA GRAS; FEMA GRAS; found in celery seeds, celery, used in baked goods, meats, soups, condiments, pickles.

108. CELLULOSE FIBER - Natural polysaccharide which is the most abundant carbohydrate in nature; found in all plant material; used in grated cheese, fruit preserves/jams, fruit jellies.

109. CHAMOMILE FLOWER OIL AND EXTRACT - FDA GRAS; FEMA GRAS; found in chamomile flowers; used in non-alcoholic beverages, ice cream, baked goods, gelatins and puddings.

110. CHICORY EXTRACT - FDA GRAS, FEMA GRAS; found in chicory; used in baked goods, non-alcoholic beverages, ice cream

111. CHOCOLATE - FDA GRAS, common food item.

112. CINNAMALDEHYDE - FDA GRAS, FEMA GRAS; found in beer, brandy, blueberries, cantaloupe, capers, cranberries, gin, guava, melon; used in gravies, candy, ice cream, meat.

113. CINNAMIC ACID - FDA approved food additive; FEMA GRAS; found in beer, blackberry, capers, cherry, grape, guava, malt, mango, mushroom, passion fruit, strawberry; used in soft candy.

114. CINNAMON LEAF OIL, BARK OIL, AND EXTRACT - FDA GRAS; FEMA GRAS; found in cinnamon tree; used in baked goods, chewing gum, candy, meats, condiments, pickles.

115. CINNAMYL ACETATE - FDA approved food additive; FEMA GRAS; found in guava; used in candy, ice cream, condiments.

116. CINNAMYL ALCOHOL - FDA approved food additive; FEMA GRAS; found in blackberry, blueberry, cantaloupe, cranberry, guava, melon, raspberry, strawberry, watermelon; used in non-alcoholic beverages.

117. CINNAMYL CINNAMATE - FDA approved food additive. FEMA GRAS: found in storax; used in baked goods, ice cream, candy.

118. CINNAMYL ISOVALERATE - FDA approved food additive; FEMA GRAS; found in chestnut flowers; used in candy, gelatin and puddings, chewing gum.

119. CINNAMYL PROPIONATE - FDA approved food additive; FEMA GRAS; used in hard candy.

120. CITRAL - FDA GRAS; FEMA GRAS; found in grapefruit juice, orange, orange juice, celery, apricot, black currants, grape, hops, kiwi fruit, mango, mango ginger, melon, plum, raspberry, rum; used in baked goods, candy, ice cream.

121. CITRIC ACID - FDA GRAS; FEMA GRAS; widely found in fruits and vegetables; used in fruit juices, meats, poultry, beverages.

122. CITRONELLA OIL - FDA GRAS; FEMA GRAS; found in citronella; used in alcoholic beverages, ice cream, baked goods.

123. dl-CITRONELLOL - FDA approved food additive; FEMA GRAS; found in apple, apricot, beer, black currants, blackberry, blueberry, orange juice, passion fruit, peach; used in soft candy.

124. CITRONELLYL BUTYRATE - FEMA GRAS; found in passion fruit, tomato; used in baked goods, candy, gelatins, puddings, non-alcoholic beverages.

125. CITRONELLYL ISOBUTYRATE - FDA approved food additive; FEMA GRAS; used in candy, gelatins and puddings, non-alcoholic beverages, baked goods.

126. CIVET ABSOLUTE - FDA GRAS; FEMA GRAS; found in civet; used in ice cream, candy, baked goods, chewing gum.

127. CLARY OIL - FDA GRAS; FEMA GRAS; found in clary sage; used in alcoholic beverages, baked goods, condiments.

128. CLOVER TOPS, RED SOLID EXTRACT - FDA GRAS; FEMA GRAS; found in clover flowers; used in jam and jelly.

129. COCOA, COCOA SHELLS, EXTRACT, DISTILLATE AND POWDER -FDA GRAS; found in cocoa, cocoa shells; used in baked goods.

130. COCONUT OIL - found in coconut; used in shortening and candies, chocolate.

131. COFFEE - FDA GRAS; found in coffee; used in baked goods, candy, syrups.

132. COGNAC WHITE AND GREEN OIL - FDA GRAS; FEMA GRAS; found in cognac brandy; used in alcoholic beverages, ice cream, baked goods.

133. COPAIBA OIL - FDA approved food addiuve; found in copaiba.

134. CORIANDER EXTRACT AND OIL - FDA GRAS; FEMA GRAS; found in coriandar; used in baked goods, meats, condiments.

135. CORN OIL - found in corn; used in baked goods, maragarine, salad oils.

136. CORN SILK - FDA GRAS; FEMA GRAS; found in corn; used in baked goods, beverages, candy, desserts.

137. COSTUS ROOT OIL - FDA approved food additive; FEMA GRAS; found in Costus root; used in candy, baked goods.

138. CUBEB OIL - FDA approved food additive; FEMA GRAS; found in Piper cubebs; used in condiment relish.

139. CUMINALDEHYDE - FDA approved food additive; FEMA GRAS; found in beef, black currants, honey, mango, bonito, grape brandy, pistacia fruit; used in baked goods, chewing gum, frozen dairy products.

140. para-CYMENE - FDA approved food additive; FEMA GRAS; found in apricot, banana, beans, bell, black currants, brandy apple, carrots, celery; used in chewing gum.

141. l-CYSTEINE - FDA GRAS; FEMA GRAS; natural constituent of protein in plants and animals; found in Pippali fruit (India); used in condiment relish; beverages, meats, baked goods, dairy products.

142. DANDELION ROOT SOLID EXTRACT - FDA GRAS; FEMA GRAS; found in dandelions; used in baked goods.

143. DAVANA OIL - FDA approved food additive; FEMA GRAS; found in Artemisia plant; used in alcoholic beverages.

144. 2-trans,4-trans-DECADIENAL - FDA approved food additive; FEMA GRAS; found in chicken, cranberry, peanut, tomato; used in vegetables, baked goods, meat, candy, chewing gum, cereals.

145. delta-DECALACTONE - FDA approved food additive; FEMA GRAS; found in apricot, beef fat, butter, black currants, blackberry, blue cheese, cheddar cheese, chicken, coconut, cranberry, cream; used in baked goods, margarine, candy.

146. gamma-DECALACTONE - FDA approved food additive; FEMA GRAS; found in apricot, beef, butter, beer, blue cheese, grape brandy, plum brandy, wheat bread, cantaloupe, cheese; used in baked goods, frozen dairy products.

147. DECANAL - FDA GRAS; FEMA GRAS; found in almond, apple, apple flowers, apricot, artichoke, avocado, beef, wheat bread; used in baked goods, beverages, ice cream, candy.

148. DECANOIC ACID - FDA approved food additive, FEMA GRAS; found in apple, apple flowers, banana, beef, beer, blackberries, blue cheese, brandies, wheat bread, butter, heated butter; used in imitation dairy goods.

149. 1-DECANOL - FDA approved food additive, FEMA GRAS; found in apple, apple juice, apricot, asparagus, banana, beer, brandy apple, butter; used in frozen dairy goods, ice cream, beverages, candy

150. 2-DECENAL - FDA approved food additive, FEMA GRAS; found in carrot root, chicken, orange, soybean; used in non-alcoholic beverages, alcoholic beverages, baked goods, candy, gelatin and puddings, dairy products.

151. DEHYDROMENTHOFUROLACTONE - FEMA GRAS; used in chewing gum.

152. DIETHYL MALONATE - FDA approved food additive; FEMA GRAS; found in whiskey, wine, blackberry, grape brandy strawberry wine.

153. DIETHYL SEBACATE - FDA approved food additive; FEMA GRAS; used in chewing gum, candy, baked goods.

154. 2,3-DIETHYLPYRAZINE - FEMA GRAS, found in wheat bread, wheat, hazelnut, baked potato, soy sauce; used in candy, gelatin and puddings.

155. DIHYDRO ANETHOLE - FEMA GRAS; used in non-alcoholic beverages, alcoholic beverages, ice cream, ices, candy, dairy products, baked goods.

156. 5,7-DIHYDRO-2-METHYLTHIENO(3,4-D) PYRIMIDINE - FEMA GRAS; used in breakfast cereals, beverages, ice cream, candy, dairy products.

157. DILL SEED OIL AND EXTRACT - FDA GRAS; FEMA GRAS; found in dill; used in cheese, meats, sauces, dips, baked goods.

158. meta-DIMETHOXYBENZENE - FDA approved food additive; FEMA GRAS; found in brandy grape, salami, filberts; used in meat products, beverages, ice cream, candy, baked goods.

159. para-DIMETHOXYBENZENE - FDA approved food additive; FEMA GRAS; found in tea, hyacinth oil, peppermint oil; used in gelatin pudding, beverages, ice cream, candy, baked goods.

160. 2,6-DIMETHOXYPHENOL - FEMA GRAS; found in maple syrup, rum, smoked sausage, wine; used in seafood, meat, baked goods, candy, soups.

161. DIMETHYL SUCCINATE - FDA approved food additive; FEMA GRAS; found in blackberry, hazelnut; used in hard candy, beverages, ice cream, candy, baked goods.

162. 3,4-DIMETHYL-1,2-CYCLOPENTANEDIONE - FEMA GRAS; found in roasted coffee; used in nut products, beverages, ice cream, candy.

163. 3,5-DIMETHYL-1,2-CYCLOPENTANEDIONE - FEMA GRAS; found in roasted coffee; used in soft candy.

164. 3,7-DIMETHYL-1,3,6-OCTATRIENE - FDA approved food additive; FEMA GRAS; found in apricot, guava, pineapple, tomato; used in frozen dairy goods.

165. 4,5-DIMETHYL-3-HYDROXY-2,5-DIHYDROFURAN-2-ONE - FEMA GRAS; found in almond, asparagus, wheat bread, butter, chicken, steamed clam, cocoa, coconut, coffee, corn; used in baked goods, sweet sauce.

166. 6,10-DIMETHYL-5,9-UNDECADIEN-2-ONE - FDA approved food additive; FEMA GRAS; found in almond, asparagus, beans, beef, beer, cashew nuts, parmesan cheese, chicken; used in baked goods, candy, dairy products.

167. 3,7-DIMETHYL-6-OCTENOIC ACID - FEMA GRAS; found in peppermint oil; used in baked goods.

168. 2,4-DIMETHYLACETOPHENONE - FDA approved food additive; FEMA GRAS; found in coffee; used in baked goods.

169. alpha,para-DIMETHYLBENZYL ALCOHOL - FEMA GRAS; used in non-alcoholic beverages, ice cream, ices, candy.

170. alpha,alpha-DIMETHYLPHENETHYL ACETATE - FDA approved food additive; FEMA GRAS; found in apricots, black currants, custard apple, grapefruit, pineapples, peppermint, nectarines; used in soft candy, baked goods, chewing gum.

171. alpha,alpha-DIMETHYLPHENETHYL BUTYRATE - FDA approved food additive; FEMA GRAS; found in Sake; used in frozen dairy goods, beverages, candy, baked goods.

172. 2,3-DIMETHYLPYRAZINE - FEMA GRAS: found in asparagus, peanut, coffee, potato; used in gravies, beverages, candy, baked goods.

173. 2,5-DIMETHYLPYRAZINE - FEMA GRAS; found in beef, blackberry, grape brandy, cantaloupe, corn, endive, grapefruit juice, used in breakfast cereal.

174. 2,6-DIMETHYLPYRAZINE - FEMA GRAS, found in citronella, camphor oil; used in milk products, meat, candy

175. DIMETHYLTETRAHYDROBENZOFURANONE - FEMA GRAS; found in dried bonito, black and green tea, wine, used in chewing gum.

176. delta-DODECALACTONE - FDA approved food additive; FEMA GRAS; found in beef, butter, milk, blue cheese, cheddar cheese, chicken, coconut, lamb/mutton, peach, plum, pork; used in meat products, baked goods, candy.

177. gamma-DODECALACTONE - FDA approved food additive; FEMA GRAS; found in apricot, beef, beer, blackberry, blue cheese, butter, carambola (starfruit), cheddar cheese, chervil, chicken; used in baked goods, beverages, ice cream, candy.

178. para-ETHOXYBENZALDEHYDE - FDA approved food additive; FEMA GRAS; used in baked goods, beverages, ice cream, candy.

179. ETHYL 10-UNDECENOATE - FDA approved food additive; FEMA GRAS; used in baked goods, beverages, ice cream, candy.

180. ETHYL 2-METHYLBUTYRATE - FDA approved food additive; FEMA GRAS; found in apple, apple juice, beer, bilberry, blackberry, brandy apple, brandy grape, cantaloupe, fig, grape, honeydew melon; used in hard candy, beverages, ice cream.

181. ETHYL ACETATE - FDA GRAS, FEMA GRAS; found in apple, apple juice, banana, beans, beef, beer, blue cheese, blueberry; used in chewing gum, beverages, ice cream, candy.

182. ETHYL ACETOACETATE - FDA approved food additive; FEMA GRAS; found in passion fruit, sherry, strawberry, wine; used in soft candy.

183. ETHYL ALCOHOL - FDA GRAS; FEMA GRAS; found in apple, banana, bread, coffee, cucumber, potato. As required by BATF regulations, nicotine sulfate is used to denature the alcohol, which is used as a solvent to apply flavors during processing. There is no measurable effect on the nicotine level of the finished cigarette as a result of this process.

184. ETHYL BENZOATE - FDA approved food additive; FEMA GRAS; found in apple, apricot, arctic bramble, babaco fruit, banana, beer, bell, bilberry, bilberry wine, black currants, blackberry, brandy apple; used in gelatin pudding, beverages, ice cream, candy.

185. ETHYL BUTYRATE - FDA GRAS; FEMA GRAS; found in apple, apple juice, banana, beer, apricot, beef, blue cheese, brandy; used in chewing gum.

186. ETHYL CINNAMATE - FDA approved food additive; FEMA GRAS; found in beer, blackberry, brandy apple; used in baked goods, beverages, ice cream, candy.

187. ETHYL DECANOATE - FDA approved food additive; FEMA GRAS; found in apple juice, banana, beef, wheat bread, butter, cheddar cheese; used in frozen dairy goods, ice cream, candy.

188. ETHYL FENCHOL - FEMA GRAS; used in baked goods, chewing gum, dairy products.

189. ETHYL FUROATE - found in cocoa, almonds; beer, guava, kiwi fruit, papaya, white wine; used in processed meats.

190. ETHYL HEPTANOATE - FDA approved food additive; FEMA GRAS; found in cashew apple, cocoa, grape, grapefruit juice, hazelnut roasted, hops, milk, olive, papaya mountain, passion fruit, peach; used in chewing gum.

191. ETHYL HEXANOATE - FDA approved food additive; FEMA GRAS; found in banana, beer, cheese, beef, black currants, blackberry, brandies, broccoli; used in baked goods, ice cream, candy.

192. ETHYL ISOVALERATE - FDA approved food additive; FEMA GRAS; found in banana, celery, apple, beer, brandy, cantaloupes, cashew apple, parmesan cheese; used in condiments, ice cream, baked goods.

193. ETHYL LACTATE - FDA approved food additive; FEMA GRAS; found in apple, beer, cocoa, pineapple, apricot, bilberry wine, brandy, butter, capers, chicken, meat, elderberry, elderberry juice, grape, peas, plum; used in chewing gum, ice cream, baked goods.

194. ETHYL LAURATE - FDA approved food additive; FEMA GRAS; found in apple, beer, cheddar cheese, apricot, bilberry wine, blackberry, brandy, wheat bread, butter; used in baked goods, candy, ice cream.

195. ETHYL LEVULINATE - FDA approved food additive; FEMA GRAS; found in bilberry wine, brandy grape, wheat bread, cherimoya, cocoa, onion roasted, rum, wine; used in frozen dairy goods, beverages, candy, baked goods.

196. ETHYL MALTOL - FDA approved food additive; FEMA GRAS; found in apple juice; used in sweet sauce, soups, meat, candy.

197. ETHYL METHYL PHENYLGLYCIDATE - FDA GRAS; FEMA GRAS; used in condiment relish, beverages, candy, ice cream.

198. ETHYL MYRISTATE - FDA approved food additive; FEMA GRAS; found in cheddar cheese, grape wine, Bartlett pear; used in non-alcoholic beverages, alcoholic beverages, ice cream, ices, candy, baked goods.

199. ETHYL NONANOATE - FDA approved food additive; FEMA GRAS; found in apple, apricot, banana, beef, beer, bilberry wine, brandy apple, wheat bread, cocoa, elderberry, grape, nectarine, olive, peach; used in baked goods, beverages, ice cream, candy.

200. ETHYL OCTADECANOATE - FEMA GRAS; found in grapes, beer, brandy, maple syrup; used in non-alcoholic beverages, ice cream, ices, candy, alcoholic beverages.

201. ETHYL OCTANOATE - FDA approved food additive; FEMA GRAS; found in apple, banana, beer, blue cheese, apricot, bilberry wine, blackberry, brandy, wheat bread, broccoli, butter, capers; used in frozen dairy goods.

202. ETHYL OLEATE - FDA approved food additive; FEMA GRAS; found in melons, grapes, brandy, maple syrup; used in non-alcoholic beverages, candy, baked goods, gelatins and puddings, condiments and relishes.

203. ETHYL PALMITATE - FEMA GRAS; found in cheddar cheese, maple syrup, grape wine; used in nut products.

204. ETHYL PHENYLACETATE - FDA approved food additive; FEMA GRAS; found in apple, crisp bread, honey, beer, beli, bilberry wine, brandy, wheat bread, cantaloupe, chempedak fruit, cocoa, grape, grapefruit juice, guava, licorice, melon; used in gelatin and puddings, syrups, baked goods.

205. ETHYL PROPIONATE - FDA approved food additive; FEMA GRAS; found in apples, apricot, banana, beer, bilberry, blackberry, brandy, cantaloupe, cheddar cheese, cocoa, fig, grape, guava; used in baked goods, meat products, ice cream.

206. ETHYL SALICYLATE - FDA approved food additive; FEMA GRAS; found in strawberries, raspberries, wine, blackberry, brandy, mountain papaya, rum; used in baked goods, ice cream, chewing gum.

207. ETHYL trans-2-BUTENOATE - FDA approved food additive; FEMA GRAS; found in apples, cocoa, plum brandy, cantaloupe, cashews, dalieb fruit, grape, guava, kiwi fruit, mango, papaya; used in candy, baked goods.

208. ETHYL VALERATE - FDA approved food additive; FEMA GRAS; found in apple, banana, grape, apricot, bilberry wine, black currants, brandy, cashew apples, parmesan cheese, fig, guava, honey, kiwi fruit, melon, muskmelon; used in chewing gum, baked goods, beverages.

209. ETHYL VANILLIN - FDA GRAS. FEMA GRAS; found in vanilla beans; used in alcoholic beverages, imitation vanilla extract, breakfast cereals.

210. 2-ETHYL(OR METHYL)-(3.5 AND 6)-METHOXYPYRAZINE - FEMA GRAS; found in coffee, potato sprouts, used in baked goods, candy, ice cream.

211. 2-ETHYL-1-HEXANOL - FEMA GRAS, used in Non-alcoholic beverages, ice cream, ices, candy, chewing gum

212. 3-ETHYL-2-HYDROXY-2-CYCLOPENTEN-1-ONE - FEMA GRAS; found in coffee, maple syrup, peanuts, pork, used in baked goods, soups, cereals, condiments, milk and dairy products

213. 2-ETHYL-3,(5 OR 6)-DIMETHYLPYRAZINE - FEMA GRAS; found in beef, coffee, bread; used in baked goods, cereals, candy, dairy products.

214. 5-ETHYL-3-HYDROXY-4-METHYL-2(5H)-FURANONE - FEMA GRAS; nature identical by FEMA; found in beef, beer, wheat bread, cashew nuts, chicken, cocoa, coconut, coffee, crayfish, eggs, hazelnut, used in chewing gum, meat products.

215. 2-ETHYL-3-METHYLPYRAZINE - FEMA GRAS; found in beef, whole egg, chicken, heated corn oil, krill, lamb/mutton, boiled-shrimp, fermented soy sauce; used in candy, ice cream, beverages.

216. 4-ETHYLBENZALDEHYDE - FEMA GRAS; found in oranges, carrots, broccoli, tomatoes; used in Baked goods, meat products, candy, gelatins and puddings, confectionery/frosting, cereals, dairy products.

217. 4-ETHYLGUAIACOL - FDA approved food additive; FEMA GRAS; found in coffee, cranberry, smoked pork, rum, smoked sausage, tea, wine; used in non-alcoholic beverages, ice cream, ices.

218. para-ETHYLPHENOL - FEMA GRAS; found in cocoa, coffee, peanut, tomato, wine; used in baked goods, candy, gelatin and puddings, meat products.

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219. 3-ETHYLPYRIDINE - FEMA GRAS; found in Beef, chicken, coffee, corn oil, almond, barley, beer, wheat bread, cocoa, eggs; used in candy, ice cream, meat, baked goods.

220. EUCALYPTOL - FDA approved food additive; FEMA GRAS; found in black currants, blueberries, brandy, cantaloupe, cheese, cocoa, grapes, thyme, babaco fruit, bilberry, corn; used in chewing gum, ice cream, baked goods.

221. FARNESOL - FDA approved food additive; FEMA GRAS; found in oranges, lemon grass; used in non-alcoholic beverages, ice cream, candy, baked goods, gelatins and puddings.

222. D-FENCHONE - FDA approved food additive; FEMA GRAS; found in anise, basil, fennel, peppermint, saffron, thyme; used in ice cream, candy, baked goods.

223. FENNEL SWEET OIL - FDA GRAS; FEMA GRAS; found in fennel seeds; used in candy, alcoholic beverages, meats.

224. FENUGREEK, EXTRACT, RESIN, AND ABSOLUTE - FDA GRAS; FEMA GRAS; found in fenugreek; used in non-alcoholic beverages, gelatin and puddings, syrups.

225. FIG JUICE CONCENTRATE - Common food item; found in figs.

226. FOOD STARCH MODIFIED - FDA approved food additive; widespread; used in cured pork.

227. FURFURYL MERCAPTAN - FEMA GRAS; found in coffee, beef, chicken, meat, popcorn; used in non-alcoholic beverages, ice cream, ices, candy, baked goods, gelatins and puddings, icings.

228. 4-(2-FURYL)-3-BUTEN-2-ONE - FEMA GRAS; found in coffee; used in non-alcoholic beverages, ice cream, ices, candy, baked goods, gelatins and puddings, alcoholic beverages.

229. GALBANUM OIL - FDA approved food additive; FEMA GRAS; found in galbanum; used in meat products, baked goods, ice cream.

230. GENET ABSOLUTE - FDA approved food additive; FEMA GRAS; found in genet flowers; used in candy, baked goods, chewing gum.

231. GENTIAN ROOT EXTRACT - FEMA GRAS; found in Gentian root; used in non-alcoholic beverages, ice cream, ices, candy, baked goods, alcoholic beverages.

232. GERANIOL - FDA GRAS; FEMA GRAS; found in apples, apricot, beer, bilberry, black currants, blackberries; used in baked goods, candy, ice cream.

233. GERANIUM ROSE OIL - FDA GRAS, FEMA GRAS; found in geranium leaves and stems; used in chewing gum, ice cream, baked goods.

234. GERANYL ACETATE - FDA GRAS, FEMA GRAS; found in celery, cocoa, black currants, chervil, gin, ginger, grape, grapefruit juice, orange juice, passion fruit, pineapple, plum; used in baked goods, ice cream, syrups.

235. GERANYL BUTYRATE - FDA approved food additive; FEMA GRAS; found in celery, tomatoes, passion fruit; used in gelatins and puddings, ice cream, candy.

236. GERANYL FORMATE - FDA approved food additive; FEMA GRAS; found in hops, black and green tea; used in baked goods, ice cream, candy.

237. GERANYL ISOVALERATE - FDA approved food additive; FEMA GRAS; used in Non-alcoholic beverages, ice cream, ices, candy, baked goods, gelatins and puddings, chewing gum.

238. GERANYL PHENYLACETATE - FDA approved food additive; FEMA GRAS; found in Olibanum resin, sativa japonica; used in gelatins and puddings, baked goods, ice cream.

239. GINGER OIL AND OLEORESIN - FDA GRAS; FEMA GRAS; found in ginger; used in candy, baked goods, meats

240. l-GLUTAMIC ACID - FDA GRAS, FEMA GRAS; natural constituent of proteins in plants and animals; used in baked goods, meat, soups, milk/dairy products, condiments, pickles, cereal

241. l-GLUTAMINE - FDA approved food additive; FEMA GRAS; natural constituent of proteins in plants and animals; used in baked goods, meat products, candy, nut products, seasonings and flavorings.

242. GLYCEROL - FDA GRAS; FEMA GRAS; found in beer, cherry, wine; used in milk products, baked goods, meat products.

243. GLYCYRRHIZIN AMMONIATED - FDA GRAS; FEMA GRAS; found in licorice; used in non-alcoholic beverages, candy, baked goods, chewing gum, ice cream, ices.

244. GRAPE JUICE CONCENTRATE - common food item; found in grapes.

269. HEXYL ACETATE - FDA approved food additive; FEMA GRAS; found in apples, bananas, beer, apricot, beef, black currants, blackberry, blueberry, brandy, cantaloupe, capers; coffee; used in candy, baked goods, meat products.

270. HEXYL ALCOHOL - FDA approved food additive; FEMA GRAS; found in apple, banana, beef, chicken, coffee, pineapple, potato; used in baked goods, gelatin and puddings, dairy products.

271. HEXYL PHENYLACETATE - FDA approved food additive; FEMA GRAS; found in grape, tea, scotch spearmint, black and green tea; used in frozen dairy goods, candy, baked goods.

272. l-HISTIDINE - FEMA GRAS; found in milk, cheese, grains, meats, poultry, eggs, fish, vegetables, nuts, fruit; used in baked goods, meat products, milk products, confectionery and frosting.

273. HONEY - common food item.

274. HOPS OIL - FDA GRAS; FEMA GRAS; used in gelatin pudding, chewing gum, baked goods.

275. HYDROLYZED MILK SOLIDS - USDA approved meat flavor; found in milk; used in meats, sauces and stuffings.

276. HYDROLYZED PLANT PROTEINS - FDA GRAS; found in plants; used in baked goods, milk and dairy products, meat products, baby formulas, soups, condiments and relishes.

277. 5-HYDROXY-2,4-DECADIENOIC ACID delta-LACTONE - FEMA GRAS; found in peaches, beef; used in chewing gum, cheese, condiments.

278. 4-HYDROXY-2,5-DIMETHYL-3(2H)-FURANONE - FEMA GRAS; found in beef, maple syrup, cassia oil; used in frozen dairy goods, baked goods, candy.

279. 2-HYDROXY-3,5,5-TRIMETHYL-2-CYCLOHEXEN-1-ONE - FEMA GRAS; found in rose oil, gardenia; used in frozen dairy goods, candy.

280. 4-HYDROXY-3-PENTENOIC ACID LACTONE - FEMA GRAS; found in bread, grapes, soy beans; used in ice cream, ices, candy, baked goods, gelatins and puddings, meat, meat sauces, soups, milk and dairy products, cereals.

281. 2-HYDROXY-4-METHYLBENZALDEHYDE - FEMA GRAS; found in blackberry, capers, cranberry, raspberry, sea buckthorn; used in baked goods.

245. GUAIAC WOOD OIL - FDA approved food additive; FEMA GRAS; found in guaiac wood; used in meat products, ice cream, chewing gum.

246. GUAIACOL - FDA approved food additive; FEMA GRAS; found in celery, cocoa, coffee, rum, soybean, tea, tomato, whiskey, wine; used in ice cream, ices, baked goods, meat, chewing gum, dairy products.

247. GUAR GUM - FEMA GRAS; found in the seed of the guar plant which is similar to the soybean plant; used in breakfast cereal, dairy products, gravies, processed vegetables, baked goods.

248. 2,4-HEPTADIENAL - FEMA GRAS; found in avocado, beef, black currants, bread, wheat, broccoli, butter, heated butter, cabbage, cauliflower; used in meat products, baked goods, soups, candy.

249. gamma-HEPTALACTONE - FDA approved food additive; FEMA GRAS; found in mango, passion fruit, peach, black tea, asparagus, butter, hazelnut, lamb/mutton, leek, licorice, nectarine, papaya, pineapple; used in candy, baked goods, ice cream.

250. HEPTANOIC ACID - FDA approved food additive; FEMA GRAS; found in apple, beer, banana, beef, dried blue cheese, brandy, bread, wheat butter, cheddar cheese; used in baked goods, margarine, ice cream.

251. 2-HEPTANONE - FDA approved food additive; FEMA GRAS; found in apples, banana, beer, beef, apricot, asparagus, beans, blue cheese, wheat butter; used in gravies, ice cream, condiments, baked goods.

252. 3-HEPTEN-2-ONE - FEMA GRAS; found in capsicum peppers, hazelnut, hops, muruci; used in gelatin and puddings, ice cream, baked goods.

253. 2-HEPTEN-4-ONE - FEMA GRAS; found in roasted filbert; used in non-alcoholic beverages, ice cream, ices, baked goods, candy, gelatin and puddings, dairy products.

254. 4-HEPTENAL - FDA approved food additive; FEMA GRAS; found in butterfat, soybean oil; used in Non-alcoholic beverages, baked goods, meat, candy, cereal, dairy products.

255. trans-2-HEPTENAL - FEMA GRAS; found in apple, chicken, cranberry, green pea, potato, tomato; used in Baked goods, meat, meat sauces, soups, candy.

256. HEPTYL ACETATE - FEMA GRAS; found in apples, grapes, bananas, pears, plums, whiskey; used in baked goods, gelatins and puddings, chewing gum.

257. omega-6-HEXADECENLACTONE - FDA approved food additive; FEMA GRAS; found in Ambrette seed; used in baked goods, ice cream, candy.

258. gamma-HEXALACTONE - FDA approved food additive; FEMA GRAS; found in apricot, beef, butter, apple, asparagus, beer, blackberry, brandy, wheat bread; used in candy, baked goods, ice cream.

259. HEXANAL - FDA approved food additive, FEMA GRAS; found in apples, bananas, beef, bilberries, apricot, artichoke, asparagus, avocado, barley, beer, blackberry, blueberry, others; used in frozen dairy goods, baked goods, meat.

260. HEXANOIC ACID - FDA approved food additive; FEMA GRAS; found in apple, beef, beer, apricot, banana, barley, blackberry, blue cheese, blueberry, bread, wheat; used in condiment relish, ice cream, candy.

261. 2-HEXEN-1-OL - FDA approved food additive, FEMA GRAS; found in apples, apricots, bananas, beer, Swiss cheese, peaches, used in Non-alcoholic beverages, candy, baked goods, gelatins and puddings.

262. 3-HEXEN-1-OL - FDA approved food additive; FEMA GRAS; found in apple, banana, bean, celery, grape, apricot cantaloupe, pineapple, honeydew melon; used in chewing gum, ice cream, candy, baked goods

263. cis-3-HEXEN-1-YL ACETATE - FEMA GRAS; found in apple juice, apricot, artichoke, asparagus, avocado, banana, beans, beef, beer, blackberry, blueberry, dried bonito, grape brandy, wheat bread, used in ices, candy, baked goods.

264. 2-HEXENAL - FDA approved food additive, FEMA GRAS; found in apple, banana, raspberry, strawberry, beer, chicken, fat, grape, guava, hops, peach, pork, black and green tea; used in frozen dairy goods, baked goods, candy.

265. 3-HEXENOIC ACID - FEMA GRAS; found in banana, pork fat, raspberry, black tea; used in non-alcoholic beverages, ice cream, dairy products, candy, chewing gum.

266. trans-2-HEXENOIC ACID - FEMA GRAS; found in apples, bananas, beer, apple juice, artichoke, beans, beef, blackberry, blueberry; used in beverages, candy, baked goods, gelatins and puddings, frozen desserts.

267. cis-3-HEXENYL FORMATE - FEMA GRAS; found in tea, cognac; used in baked goods, chewing gum, preserves and spreads.

268. HEXYL 2-METHYLBUTYRATE - FDA approved food additive; FEMA GRAS; found in apples, strawberries, apricot, apple brandy, grape, Asian pear, plum, native spearmint; used in gelatins and puddings, candy, ice cream.

282. 4-HYDROXYBUTANOIC ACID LACTONE - FEMA GRAS; found in apricots, bread, coffee, cocoa, mushroom, onion, wine; used in dairy products, breakfast cereals, meat products.

283. HYDROXYCITRONELLAL - FDA approved food additive; FEMA GRAS; found in beef, mushroom, nectarine, peach; used in candy, ice cream, baked goods.

284. 6-HYDROXYDIHYDROTHEASPIRANE - FEMA GRAS; found in black tea; used in non-alcoholic beverages, ice cream, candy, gelatin and puddings.

285. 4-(para-HYDROXYPHENYL)-2-BUTANONE - FDA approved food additive; FEMA GRAS; found in almond, beef, coffee, grape, guava, hazelnut, pineapple, popcorn, raspberry, soy sauce, strawberry; used in chewing gum, ice cream, baked goods.

286. HYSSOP OIL - FDA GRAS; FEMA GRAS; used in alcoholic beverages, ice cream, candy, baked goods.

287. IMMORTELLE ABSOLUTE AND EXTRACT - FDA GRAS; FEMA GRAS; used in baked goods, candy, gelatin and puddings, chewing gum, frozen dairy products.

288. alpha-IONONE - FDA approved food additive; FEMA GRAS; found in raspberry, almond, banana, blackberry, grape brandy, raspberry brandy, capers, carrots, celery, cherry, grapefruit juice, kumazasa, mango ginger, peach, peas, plum; used in chewing gum., ice cream, baked goods

289. beta-IONONE - FDA approved food additive; FEMA GRAS; found in carrot, almonds, apricot, beer, blackberry, brandy, broccoli, capers, cherry, endive; used in candy, baked goods, ice cream.

290. alpha-IRONE - FDA approved food additive; FEMA GRAS; found in raspberry; used in baked goods, frozen dairy, soft candy, gelatin and puddings, alcoholic beverages.

291. ISOAMYL ACETATE - FDA approved food additive; FEMA GRAS; found in apple, banana, beer, apricot, blackberry, blackberry brandy, wheat bread, butter; used in chewing gum, ice cream, baked goods.

292. ISOAMYL BENZOATE - FDA approved food additive; FEMA GRAS; found in beer, cherries, cocoa, papaya; used in baked goods, candy, gelatin and puddings.

293. ISOAMYL BUTYRATE - FDA approved food additive; FEMA GRAS; found in banana, blue cheese, grape, apple, apricot, beer, apple brandy, grape brandy, guava, honey, mango; used in non-alcoholic beverages, ice cream, baked goods, chewing gum.

294. ISOAMYL CINNAMATE - FDA approved food additive; FEMA GRAS; found in wine, cinnamon, styrax; used in baked goods, candy, gelatin and puddings.

295. ISOAMYL FORMATE - FDA approved food additive; FEMA GRAS; found in apple, beer, chicken, honey, eggs, rum, strawberries, tea, vinegar, grape brandy, whiskey, wine; used in baked goods, candy

296. ISOAMYL HEXANOATE - FDA approved food additive; FEMA GRAS; found in apple, apricot, banana, grapefruit juice, plums, strawberries, beer, grape brandy, plum brandy, rum, sherry; used in candy, chewing gum.

297. ISOAMYL ISOVALERATE - FDA approved food additive; FEMA GRAS; found in banana, tomato, beer, sherry, spearmint, scotch; used in frozen dairy goods, candy.

298. ISOAMYL OCTANOATE - FDA approved food additive; FEMA GRAS; found in banana, beer, grape, strawberry, used in baked goods, soft candy, gelatin and puddings, alcoholic beverages

299. ISOAMYL PHENYLACETATE FDA approved food additive; FEMA GRAS; found in peppermint oil; used in baked goods, candy, chewing gum.

300. ISOBORNYL ACETATE - FDA approved food additive; FEMA GRAS; found in Kiwi fruit; used in soft candy

301. ISOBUTYL ACETATE - FDA approved food additive; FEMA GRAS; found in apples, bananas, cantaloupe, cocoa, figs, honeydew melon, beer, grape, guava, mango, melon; used in chewing gum, gelatin and puddings.

302. ISOBUTYL ALCOHOL - FDA approved food additive; FEMA GRAS; found in beef, blackberry, apple, apricot, banana, barley, brandy; used in gelatin and puddings, candy, baked goods.

303. ISOBUTYL CINNAMATE - FDA approved food additive; FEMA GRAS; found in coffee, tomato, mullein leaves; used in candy, ice cream, baked goods.

304. ISOBUTYL PHENYLACETATE - FDA approved food additive; FEMA GRAS; found in cocoa; used in baked goods, ice cream, candy.

305. ISOBUTYL SALICYLATE - FDA approved food additive; FEMA GRAS; found in Feijoa fruit; used in soft candy, baked goods.

306. 2-ISOBUTYL-3-METHOXYPYRAZINE - FEMA GRAS; found in bean, coffee, pea, pepper, potato, spinach, grape; used in non-alcoholic beverages, ice crem, dairy products.

307. alpha-ISOBUTYLPHENETHYL ALCOHOL - FDA approved food additive; FEMA GRAS; used in non-alcoholic beverages, alcoholic beverages, ice cream, ices, candy, gelatin and puddings, baked goods.

308. ISOBUTYRALDEHYDE - FDA approved food additive; FEMA GRAS; found in apple, banana, barley, beans, beef, beer, blue cheese, brandy, bread, wheat, butter; used in gelatin and puddings, candy, frozen dairy products.

309. ISOBUTYRIC ACID - FDA approved food additive; FEMA GRAS; found in apple, beef, beer, celery, banana, blue cheese, grape brandy, wheat bread, cashew apples, cheddar cheese; used in baked goods, candy, gelatin and puddings.

310. d,l-ISOLEUCINE - FEMA GRAS; natural constituent of protein in plants and animals; used in milk products, meat products, condiment relish, soups.

311. alpha-ISOMETHYLIONONE - FDA approved food additive; FEMA GRAS; used in baked goods, soft candy, gelatin and puddings, chewing gum.

312. 2-ISOPROPYLPHENOL - FEMA GRAS; found in Japanese whiskey; used in meat, soups, condiments.

313. ISOVALERIC ACID - FDA approved food additive; FEMA GRAS; found in apple, beer, banana, blue cheese, grape brandy, wheat bread, heated butter, capers, cashew apples, cheddar cheese; used in frozen dairy goods, candy, cheese.

314. JASMINE ABSOLUTE, CONCRETE and OIL - FDA GRAS; FEMA GRAS; found in Jasmine flowers; used in baked goods, chewing gum, candy.

315. KOLA NUT EXTRACT - FDA GRAS; FEMA GRAS; found in kola nut; used in gelatin pudding, ice cream, candy.

316. LABDANUM ABSOLUTE AND OLEORESIN - FDA approved food additive; FEMA GRAS; used in baked goods, frozen dairy products, gelatin and puddings.

317. LACTIC ACID - FDA GRAS; FEMA GRAS; found in apple juice, beef, beer, bread, cocoa, coffee, wheat bread, cherry, grape, guava, mango, milk, papaya, dry salami, sherry, tomato; used in cheese, candy, chewing gum, baked goods.

318. LAURIC ACID - FDA GRAS; FEMA GRAS; found in apple, beer, blue cheese, banana, beef, blackberry, brandy, wheat bread, butter, heated butter, cantaloupe, cashew nuts; used in baked goods, candy, ice cream.

319. LAURIC ALDEHYDE - FDA approved food additive; FEMA GRAS; found in apples, beef, beer, wheat bread, carrots, celery, cheddar cheese, blackberry, butter, cabbage, caviar, chicken; used in chewing gum, baked goods, candy.

320. LAVANDIN OIL - FDA GRAS; FEMA GRAS; found in lavender plant; used in baked goods, candy, chewing gum.

321. LAVENDER OIL - FDA GRAS; FEMA GRAS; found in lavender flowers; used in soft candy, baked goods, gelatin and puddings.

322. LEMON OIL AND EXTRACT - FDA GRAS; FEMA GRAS; found in lemons; used in candy, breakfast cereals, frozen dairy products.

323. LEMONGRASS OIL - FDA GRAS; FEMA GRAS; found in lemongrass; used in chewing gum, ice cream, baked goods.

324. l-LEUCINE - FDA approved food additive; FEMA GRAS; found in proteins; essential amino acid; used in soups, baked goods, breakfast cereals.

325. LEVULINIC ACID - FDA approved food additive; FEMA GRAS; found in wheat bread, papaya; used in reconstituted vegetables, ice cream, baked goods.

326. LICORICE ROOT, FLUID EXTRACT AND POWDER - FDA GRAS; FEMA GRAS; found in glycyrrhizia; used in candy, baked goods, meat products.

327. LIME OIL - FDA GRAS; FEMA GRAS; found in lime; used in frozen dairy goods, candy.

328. LINALOOL - FDA GRAS; FEMA GRAS; found in banana, beer, blackberry, beans, blueberry, apple, apricot, arctice bramble, artichoke, grape brandy, plum brandy; used in meat products.

329. LINALOOL OXIDE - FDA approved food additive; FEMA GRAS; found in oranges, apricot, coffee; used in ice cream, baked goods, candy.

330. LINALYL ACETATE - FDA GRAS; FEMA GRAS; found in bergamot, clary sage, lemon oil, pepper, tomato, lavender; used in baked goods, dairy products, candy.

331. LINDEN FLOWERS - FDA GRAS; FEMA GRAS; found in linden flowers; used in non-alcoholic beverages.

332. LOVAGE OIL AND EXTRACT - FDA approved food additive; FEMA GRAS; found in levisticum; used in sweet sauce, alcoholic beverages, ice cream.

333. l-LYSINE - FDA approved food additive; amino acid, natural constituent of plant and animal proteins; used in meat products, breakfast cereals.

334. MACE POWDER, EXTRACT AND OIL - FDA GRAS; FEMA GRAS; found in mace; used in alcoholic beverages, candy, frozen dairy products.

335. MAGNESIUM CARBONATE - FDA GRAS, used in flour, baked goods, frozen dairy products.

336. MALIC ACID - FDA GRAS; FEMA GRAS, found in celery, cocoa, orange juice, grape brandy, sour cherry, gin, grapefruit juice, honey, hops, kiwi fruit, mango, mushroom; used in frozen dairy goods, candy, baked goods.

337. MALT AND MALT EXTRACT - FDA GRAS; found in barley; used in beer, frozen dairy products, baked goods.

338. MALTODEXTRIN - FDA GRAS, used in baked goods, candy, frozen dairy.

339. MALTOL - FDA approved food additive, FEMA GRAS; found in barley, cocoa, coffee, beef, wheat bread butter, hazelnut, licorice, malt, milk, peanut; used in frozen dairy goods, jellies baked goods.

340. MALTYL ISOBUTYRATE - FEMA GRAS, used in baked goods, soft candy, gelatin and puddings, jam and jelly

341. MANDARIN OIL - FDA GRAS, FEMA GRAS; found in tangerines, mandarin oranges; used in candy, frozen dairy products.

342. MAPLE SYRUP AND CONCENTRATE - common food item.

343. MATE LEAF, ABSOLUTE, AND OIL - FDA GRAS; found in mate leaves; used in flour, meat, poultry.

344. para-MENTHA-8-THIOL-3-ONE - FEMA GRAS; used in frozen dairy, soft candy, gelatin and puddings, baked goods.

345. MENTHOL - FDA approved food additive; FEMA GRAS; found in peppermint plant, honey, mint, rum, cocoa, eggs, guava, raspberry, rice, spearmint; used in candy, mouthwash.

346. MENTHONE - FDA approved food additive; FEMA GRAS; found in celery, clams, cocoa, peppermint, raspberries, rice, spearmint; used in baked goods, candy.

347. MENTHYL ACETATE - FEMA GRAS; found in peppermint oil, orange juice, raspberries; used in baked goods, frozen dairy, soft candy, gelatin and pudding.

348. dl-METHIONINE - FDA approved food additive; FEMA GRAS; natural constituent of protein in plants and animals; used in breakfast cereals, meat products, condiment relish, soups.

349. METHOPRENE - EPA approved pesticide for use on tobacco; allowed by FDA to be used in raisins, prunes, peaches, oat cereals; also approved by EPA for eggs, milk, poultry.

350. 2-METHOXY-4-METHYLPHENOL - FDA approved food additive; FEMA GRAS; found in cocoa, sausage, banana, beer, coffee; used in baked goods, meat products.

351. 2-METHOXY-4-VINYLPHENOL - FDA approved food additive; FEMA GRAS; found in bean, coffee, sherry, whiskey, banana, beer, cocoa, cured ham, malt; used in meat products, ice cream, baked goods.

352. para-METHOXYBENZALDEHYDE - FDA approved food additive; FEMA GRAS: found in coffee, tea, tomato, beer, krill; used in baked goods, candy, dairy products.

353. 1-(para-METHOXYPHENYL)-1-PENTEN-3-ONE - FDA approved food additive; FEMA GRAS; found in jasmine, Ylang Ylang; used in soft candy, sweet sauce, baked goods.

354. 4-(para-METHOXYPHENYL)-2-BUTANONE - FDA approved food additive; FEMA GRAS; found in apricot, beer, brandy, grapes, cantaloupe, cranberry, honey, melon, peppermint, plum, raspberry, salami; used in candy, baked goods.

355. 1-(para-METHOXYPHENYL)-2-PROPANONE - FDA approved food additive; FEMA GRAS; found in chervil; used in baked goods, frozen dairy, soft candy, gelatin and puddings.

356. METHOXYPYRAZINE - FEMA GRAS: found in beef, cocoa; used in meat products, soups, gravies, baked goods.

357. METHYL 2-FUROATE - FEMA GRAS; found in almond, cocoa, coffee, peanut, wine; used in non-alcoholic beverages, ice cream, candy, baked goods.

358. METHYL 2-OCTYNOATE - FDA approved food additive; FEMA GRAS; used in baked goods, frozen dairy products, gelatin and puddings.

Source: https://www.industrydocuments.ucsf.edu/docs/tggl0001

359. METHYL 2-PYRROLYL KETONE - FEMA GRAS; found in apple juice, cocoa, coffee, onion, peanut; used in baked goods, candy, gelatin and puddings, meat products.

360. METHYL ANISATE - FDA approved food additive; FEMA GRAS; used in non-alcoholic beverages, frozen dairy, baked goods, soft candy, gelatin and puddings.

361. METHYL ANTHRANILATE - FDA GRAS; FEMA GRAS; found in cocoa, grape, tea, wine, coffee, strawberry; used in baked goods, candy, frozen dairy products.

362. METHYL BENZOATE - FDA approved food additive; FEMA GRAS; found in banana, cherry, coffee, brandy, butter, cashew apple; used in chewing gum, ice cream, candy.

363. METHYL CINNAMATE - FDA approved food additive; FEMA GRAS; found in guava, strawberry, cranberry, pineapple, plum; used in baked goods, candy, gelatin and puddings.

364. METHYL DIHYDROJASMONATE - FEMA GRAS; used in non-alcoholic beverages, ice cream, ices, baked goods, candy.

365. METHYL ESTER OF ROSIN, PARTIALLY HYDROGENATED - FDA approved food additive; used in baked goods, candy.

366. METHYL ISOVALERATE - FDA approved food additive; FEMA GRAS; found in apple, peach, pineapple, banana, blackberry, parmesan cheese, coffee, honey, nectarine, olives, peas, strawberries, used in candy, baked goods.

367. METHYL LINOLEATE (48%) METHYL LINOLENATE (52%) MIXTURE; FEMA GRAS; found in banana, grape, grapefruit juice, melon, strawberries; used in ice cream, baked goods, candy.

368. METHYL NAPHTHYL KETONE - FDA approved food additive; FEMA GRAS; found in beef (heated); used in chewing gum.

369. METHYL NICOTINATE - FEMA GRAS; found in coffee, nuts, strawberry, beef, beer, guava, hazelnuts, peanut, plum; used in baked goods, candy, ice cream.

370. METHYL PHENYLACETATE - FDA approved food additive; FEMA GRAS; found in coffee, cocoa; used in candy, syrups, baked goods.

371. METHYL SALICYLATE - FDA approved food additive; FEMA GRAS; found in blackberry, broccoli, butter, cherry cake, coffee; used in candy, ice cream, syrups.

372. METHYL SULFIDE - FDA approved food additive; FEMA GRAS; found in asparagus, bean, beef, beer, white bread, brussels sprouts, butter, cabbage, carrot, cauliflower, broccoli; used in meat products, candy, ice cream.

373. 3-METHYL-1-CYCLOPENTADECANONE - FEMA GRAS; found in grape brandy, lamb/muttonm potato; used in baked goods.

374. 4-METHYL-1-PHENYL-2-PENTANONE - FDA approved food additive; FEMA GRAS; used in gelatin pudding.

375. 5-METHYL-2-PHENYL-2-HEXENAL - FEMA GRAS; found in romano cheese, potato chips; used in soft candy.

376. 5-METHYL-2-THIOPHENECARBOXALDEHYDE - FEMA GRAS; found in coffee, roasted peanut, popcorn, cooked beef; used in baked goods, meats, soups, candy, gelatin and puddings, chewing gum, dairy products, condiments.

377. 6-METHYL-3,5-HEPTADIEN-2-ONE - FDA approved food additive; FEMA GRAS; found in almonds, asparagus, beef, beer, wheat bread, cashew nuts, chicken; used in snack foods.

378. 2-METHYL-3-(para-ISOPROPYLPHENYL) PROPIONALDEHYDE - FDA approved food additive; FEMA GRAS; found in almond, beans, beef, beer, wheat bread, chicken, cocoa, coffee, guava, macadamia nut; used in gelatin pudding.

379. 5-METHYL-3-HEXEN-2-ONE - FEMA GRAS; found in roasted filbert; used in baked goods, cereals, candy, gelatin and puddings, dairy products.

380. 1-METHYL-3-METHOXY-4-ISOPROPYLBENZENE - FEMA GRAS; found in tangerine peel, thyme; used in non-alcoholic beverages, baked goods, meat, candy, condiments.

381. 4-METHYL-3-PENTENE-2-ONE - FEMA GRAS; found in rye bread, coffee, tea, peanut; used in non-alcoholic beverages, baked goods, candy, gelatin and puddings, dairy products.

382. 2-METHYL-4-PHENYLBUTYRALDEHYDE - FEMA GRAS; used in non-alcoholic beverages, ice cream, candy, gelatin and puddings.

383. 6-METHYL-5-HEPTEN-2-ONE - FDA approved food additive; FEMA GRAS; found in guava, mango, potato, rum; used in gravies, candy, baked goods.

384. 4-METHYL-5-THIAZOLEETHANOL - FEMA GRAS; found in cocoa, malt, peanuts roasted; used in meat products.

385. 4-METHYL-5-VINYLTHIAZOLE - FEMA GRAS; found in cocoa, nuts, passion fruit; used in ice cream, baked goods, meat sauce, candy, chewing gum.

386. METHYL-alpha-IONONE - FDA approved food additive; FEMA GRAS; used in baked goods.

387. METHYL-trans-2-BUTENOIC ACID - FEMA GRAS; found in celery oil, orange juice crystals, coffee, strawberry; used in baked goods, meat products, soups.

388. 4-METHYLACETOPHENONE - FDA approved food additive; FEMA GRAS; found in hop oil, cocoa powder, black currant; used in chewing gum.

389. para-METHYLANISOLE - FDA approved food additive; FEMA GRAS; found in cocoa, malt, peanut, pork, potato chips, sesame seeds; used in baked goods.

390. alpha-METHYLBENZYL ACETATE - FDA approved food additive; FEMA GRAS; found in grape brandy, rice, tea, tomato, tomato paste; used in chewing gum.

391. alpha-METHYLBENZYL ALCOHOL - FEMA GRAS; found in mushroom, hops, grapes, endive, cranberry; used in baked goods.

392. 2-METHYLBUTYRALDEHYDE - FDA approved food additive; FEMA GRAS; found in beef, apple, cheddar cheese, coffee, cranberry, eggs, fish, lettuce, olive, onion, peas, tomato; used in gelatin pudding.

393. 3-METHYLBUTYRALDEHYDE - FDA approved food additive; FEMA GRAS; found in apple, banana, bread, tomato, rice, blackberry; used in baked goods.

394. 2-METHYLBUTYRIC ACID - FDA approved food additive; FEMA GRAS; found in apple, apricot, avocado, beef, beer, blackberry, brandy, butter, cantaloupes, carrots; used in cheese, ice cream, candy.

395. alpha-METHYLCINNAMALDEHYDE - FDA approved food additive; FEMA GRAS; found in blackberry, cauliflower, cherry, cocoa, endive, guava, honey, peach; used in candy.

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396. METHYLCYCLOPENTENOLONE - FDA approved food additive; FEMA GRAS; found in carambola (starfruit), cheese, tomato; used in breakfast cereals, baked goods, candy.
397. 2-METHYLHEPTANOIC ACID - FDA approved food additive; FEMA GRAS; found in gardenia flower oil, almonds, cocoa, coffee, soy sauce, onions; used in baked goods, ice cream, candy.

398. 2-METHYLHEXANOIC ACID - FEMA GRAS, found in apple, avocado, banana, barley, beans, beef, beer, blackberry, blue cheese, wheat bread, butter; used in baked goods, candy, gelatin and puddings

399. 3-METHYLPENTANOIC ACID - FEMA GRAS, found in apple, apricot, beer, blackberry, blueberry, wheat bread, romano cheese, chicken; used in baked goods.

400. 4-METHYLPENTANOIC ACID - FEMA GRAS, found in apple, grapes, cocoa, strawberry, tomato; used in condiment relish

401. 2-METHYLPYRAZINE - FEMA GRAS, found in peppermint oil, tomato, popcorn; used in milk products, baked goods, candy

402. 5-METHYLQUINOXALINE - FEMA GRAS, found in roasted almonds, coffee; used in frozen dairy, beverages, candy, gelatins.

403. 2-METHYLTETRAHYDROFURAN-3-ONE - FEMA GRAS; found in coffee; used in gravies.

404. (METHYLTHIO)METHYLPYRAZINE (MIXTURE OF ISOMERS); FEMA GRAS; used in baked goods, candy.

405. 3-METHYLTHIOPROPIONALDEHYDE - FEMA GRAS; found in bean, bread, cheese, cocoa bean, roasted nuts, milk, soy sauce, tomato; used in ice cream, ices, baked goods, diary products, fats/oils.

406. METHYL 3-METHYLTHIOPROPIONATE - FDA approved food additive; FEMA GRAS; found in cantaloupe, pineapple; used in candy, baked goods, beverages, syrups.

407. 2-METHYLVALERIC ACID - FDA approved food additive; FEMA GRAS; found in almond, barley, wheat bread, cocoa, coffee, hazelnut, licorice, malt, peanut, soy sauce, lamb/mutton; used in frozen dairy products, candy.

408. MIMOSA ABSOLUTE AND EXTRACT - FDA approved food additive; FEMA GRAS; found in Mimosa flowers; used in frozen dairy products.

409. MOLASSES EXTRACT AND TINCTURE - FDA GRAS; found in refined sugars; common food item.

410. MOUNTAIN MAPLE SOLID EXTRACT - FDA approved food additive; FEMA GRAS; found in mountain maple tree sap; used in baked goods.

411. MULLEIN FLOWERS - FDA approved food additive; natural flavor.

412. MYRISTALDEHYDE - FDA approved food additive; FEMA GRAS; found in apricot, cucumber; used in frozen dairy products, beverages, baked goods, gelatin.

413. MYRISTIC ACID - FDA approved food additive; FEMA GRAS; found in apple, banana, beef, beer, blackberry, brandy grape, butter, cantaloupe, cashew nuts, cheese (blue, cheddar); used in non-alcoholic beverages, candy, baked goods.

414. MYRRH OIL - FDA approved food additive; FEMA GRAS; found in myrrh; used in alcoholic beverages.

415. beta-NAPTHYL ETHYL ETHER - FEMA GRAS; used in soft candy.

416. NEROL - FDA approved food additive; FEMA GRAS; found in apricot, beer, blackberry, blueberry, brandy grape, cranberry, gin, grape, grapefruit juice, honey, hops, wine; used in frozen dairy products.

417. NEROLI BIGARDE OIL - FDA GRAS; FEMA GRAS; found in oranges; used in baked goods, candy.

418. NEROLIDOL - FDA approved food additive; FEMA GRAS; found in grapefruit, hops, lime, grapefruit oil; used in non-alcoholic beverages, ice cream, ices, candy, baked goods.

419. NONA-2-trans,6-cis-DIENAL - FEMA GRAS; found in apple, banana, beef, beer, blue cheese, cheddar cheese, brandy plum; used in frozen dairy goods.

420. 2,6-NONADIEN-1-OL - FDA approved food additive;FEMA GRAS; found in cucumber, frozen pea, whole soybean, tomato; used in baked goods, candy, gelatin and puddings, gravies.

421. gamma-NONALACTONE - FDA approved food additive; FEMA GRAS; found in beer, wheat bread, capers, cherry, chicken, clam; used in candy, baked goods, ice cream.

422. NONANAL - FDA approved food additive; FEMA GRAS; found in apricot, asparagus, beef, blackberry, wheat bread, cantaloupe, cocoa; used in baked goods.

423. NONANOIC ACID - FDA approved food additive; FEMA GRAS; found in apple, apricot, artichoke, avocado, banana, beef, beer, wheat bread; used in baked goods, candy, meat products.

424. 2-NONANONE - FDA approved food additive; FEMA GRAS; found in strawberry; used in dairy products, condiments.

425. trans-2-NONEN-1-OL - FEMA GRAS, found in asparagus, brandy grape, cucumber, melon, nectarine, plum, prickly pear, wine; used in baked goods.

426. 2-NONENAL - FEMA GRAS, found in asparagus, carrot, cherry, cucumber, egg, endive, olives, peach, peas, tomato, watermelon; used in meat products.

427. NONYL ACETATE - FDA approved food additive; FEMA GRAS; found in apple, beer, cantaloupe, grape, grapefruit juice, honeydew melon, milk, used in frozen dairy products.

428. NUTMEG POWDER AND OIL - FDA GRAS; FEMA GRAS; found in nutmeg; used in condiments, baked goods

429. OAK CHIPS EXTRACT AND OIL - FDA approved food additive; FEMA GRAS; found in oak tree wood chips, used in baked goods.

430. OAK MOSS ABSOLUTE - FDA approved food additive; FEMA GRAS; found in essential oil of lichen, oak moss, used in meat products, candy, ice cream.

431. 9,12-OCTADECADIENOIC ACID (48%) AND 9,12,15-OCTADECATRIENOIC ACID (52%), FDA GRAS; FEMA GRAS; found in potato, tomato, apple, beer, cheese, country ham; used in preserves, spreads, candy, gelatin and puddings.

432. delta-OCTALACTONE - FEMA GRAS; found in apricot, beef, blackberry, butter, cheese (blue, cheddar, parmesan), cranberry, cream, coconut; used in candy, margarine, baked goods.

433. gamma-OCTALACTONE - FDA approved food additive; FEMA GRAS; found in apricot, asparagus, beef, beer, blackberry, blue cheese, brandy grape, cantaloupe, cherry, chicken, cranberry; used in baked goods, candy, ice cream.

434. OCTANAL - FDA approved food additive; FEMA GRAS; found in apple, apricot, artichoke, avocado, beef, beer, blackberry, brandy, wheat bread, butter; used in frozen dairy products, beverages, baked goods, candy.

435. OCTANOIC ACID - FDA GRAS; FEMA GRAS; found in apple, banana, beef, blackberry, plum brandy, wheat butter, beer, blue cheese; used in snack foods, baked goods, candy.

436. 1-OCTANOL - FDA approved food additive; FEMA GRAS; found in apple, apricot, blueberry, cantaloupe, celery, cherry, fish, grape, mushroom, pear, peas, strawberry; used in chewing gum, beverages, ice cream, baked goods, candy.

437. 2-OCTANONE - FDA approved food additive; FEMA GRAS; found in apple, banana, beef, cheese, coffee, cocoa, milk, peanut, tea, wine; used in baked goods, candy, gelatin and puddings, dairy products.

438. 3-OCTEN-2-ONE - FEMA GRAS; found in roasted filbert, mushroom, dried pea, tea; used in non-alcoholic beverages, ice cream, baked goods, condiments, candy, dairy products.

439. 1-OCTEN-3-OL - FDA approved food additive; FEMA GRAS; found in mushroom, peppermint, spearmint; used in processed vegetables.

440. 1-OCTEN-3-YL ACETATE - FDA approved food additive; FEMA GRAS; found in asparagus, avocado, beef, wheat bread, cabbage, capers, caviar, butter; used in snack foods.

441. 2-OCTENAL - FEMA GRAS; found in asparagus, beer, banana, beans, blue cheese, butter, cantaloupe, capers, chicken; used in snack foods, baked goods, diary products.

442. OCTYL ISOBUTYRATE - FDA approved food additive; FEMA GRAS; found in hops, plum; used in baked goods, beverages, ice cream, candy.

443. OLEIC ACID - FDA approved food additive; FEMA GRAS; found in apple, banana, grape, ginger, potato, strawberry, tomato; used in condiment relish, citrus fruit, yeast, sugar beets.

444. OLIBANUM OIL - FDA approved food additive; FEMA GRAS; found in gum resin exudate; used in Non-alcoholic beverages, ice cream, ices, candy, baked goods.

445. OPOPONAX OIL AND GUM - FDA approved food additive; found in opoponax, opoponas; natural flavor; used in alcoholic beverages.

446. ORANGE BLOSSOMS WATER, ABSOLUTE AND LEAF ABSOLUTE -FDA GRAS; FEMA GRAS; found in oranges; used in non-alcoholic beverages, ice cream, ices, candy, baked goods.

447. ORANGE OIL AND EXTRACT - FDA GRAS; FEMA GRAS; found in oranges; used in non-alcoholic beverages, ice cream, ices, baked goods, condiments, candy, gelatin and puddings, chewing gum.

448. ORIGANUM OIL - FDA GRAS; FEMA GRAS; found in origanum flowers; used in soups.

449. ORRIS CONCRETE OIL AND ROOT EXTRACT - FDA approved food additive; FEMA GRAS; found in orris roots; used in gelatin pudding, alcoholic beverages.

450. PALMAROSA OIL - FDA GRAS; FEMA GRAS; found in geranium; used in baked goods.

451. PALMITIC ACID - FEMA GRAS; found in apple, beer, celery, cheddar cheese, milk, potato, tomato; used in meat products, baked goods.

452. PARSLEY SEED OIL - FDA GRAS; FEMA GRAS; found in parsley; used in soups.

453. PATCHOULI OIL - FDA approved food additive; FEMA GRAS; found in dried leaves of *Pogostemon* cablin Benth.; used in non-alcoholic beverages, ice cream, ices, baked goods, candy, chewing gum.

454. omega-PENTADECALACTONE - FDA approved food additive; FEMA GRAS; used in baked goods; ice cream, candy.

455. 2,3-PENTANEDIONE - FDA approved food additive; FEMA GRAS; found in nuts, beef, beer, bread, chicken, cocoa, coffee, tomato, yogurt; used in baked goods, candy, gelatin and puddings.

456. 2-PENTANONE - FDA approved food additive; FEMA GRAS; found in apple juice, banana, beef, cheese, chicken, grape, ham, honey, peanut; used in non-alcoholic beverages, ice cream, ices, candy, baked goods.

457. 4-PENTENOIC ACID - FDA approved food additive; FEMA GRAS; used in soft candy, beverages, baked goods, margarine.

458. 2-PENTYLPYRIDINE - FEMA GRAS; found in cooked meat, peppers, hazel nut, roasted peanuts; used in candy, baked goods, ice cream.

459. PEPPER OIL, BLACK AND WHITE - FDA GRAS; FEMA GRAS; found in pepper corns; used in condiments, ice cream, baked goods.

460. PEPPERMINT OIL - FDA GRAS; FEMA GRAS; found in peppermint; used in chewing gum, meat products, ice cream, baked goods.

461. PERUVIAN (BOIS DE ROSE) OIL - FDA GRAS; FEMA GRAS; used in baked goods, candy, chewing gum.

462. PETITGRAIN ABSOLUTE, MANDARIN OIL AND TERPENELESS OIL; FDA GRAS; FEMA GRAS; found in bitter orange tree, leaves, and twigs, oranges; used in baked goods, condiments, candy.

463. alpha-PHELLANDRENE - FDA approved food additive; FEMA GRAS; found in apple, gin, hops, mango, nectarine, papaya, paprika, parsley, beans, carrots; used in milk products, baked goods, candy

464. 2-PHENETHYL ACETATE - FDA approved food additive; FEMA GRAS; found in apple, banana, beer, brandy, raspberry, wheat bread, butter, cantaloupe; used in candy, ice cream, baked goods

465. PHENETHYL ALCOHOL - FDA approved food additive; FEMA GRAS; found in apple juice, banana, beef, beer, blackberry, blueberry, apple, apricot, asparagus; used in chewing gum, ice cream, baked goods.

466. PHENETHYL BUTYRATE - FDA approved food additive; FEMA GRAS; found in beer, banana, apple brandy, grape, strawberry, wine; used in baked goods, candy, ice cream.

467. PHENETHYL CINNAMATE - FEMA GRAS; used in non-alcoholic beverages, alcoholic beverages, ice cream, ices, baked goods, candy, gelatin and puddings.

468. PHENETHYL ISOBUTYRATE - FDA approved food additive; FEMA GRAS; found in beer, brandy, grape, olive, rum, used in chewing gum, baked goods, candy.

469. PHENETHYL ISOVALERATE - FDA approved food additive; FEMA GRAS; found in peppermint, spearmint, banana, beer, brandy, grape; used in chewing gum, candy, frozen dairy products.

470. PHENETHYL PHENYLACETATE - FDA approved food additive; FEMA GRAS; used in baked goods, candy, cheese.

471. PHENETHYL SALICYLATE - FDA approved food additive; FEMA GRAS; used in non-alcoholic beverages, alcoholic beverages, frozen dairy, baked goods, soft candy, gelatin and puddings.

472. 1-PHENYL-1-PROPANOL - FDA approved food additive; FEMA GRAS; found in beer, chicken broth, grape brandy, cocoa, guava, honey, lamb/mutton, mushroom; used in chewing gum, candy, baked goods.

473. 3-PHENYL-1-PROPANOL - FDA approved food additive; FEMA GRAS; found in cinnamon, honey, tea; used in frozen dairy, baked goods, soft candy, gelatin and puddings, chewing gum.

474. 2-PHENYL-2-BUTENAL - FEMA GRAS; found in beer, chicken, tomato, almonds, asparagus, cocoa, tea, hazelnuts; used in gelatin and puddings, candy, ice cream.

475. 4-PHENYL-3-BUTEN-2-OL - FDA approved food additive; FEMA GRAS; used in non-alcoholic beverages, frozen dairy, baked goods, soft candy, gelatin and puddings.

476. 4-PHENYL-3-BUTEN-2-ONE - FDA approved food additive; FEMA GRAS; found in beer, grape brandy, grape, guava, licorice, mango, mushroom, papaya, raspberry, strawberry, whiskey, wine; used in baked goods, candy.

477. PHENYLACETALDEHYDE - FDA approved food additive; FEMA GRAS; found in chicken, strawberry; used in baked goods, ice cream, candy.

478. PHENYLACETIC ACID - FDA approved food additive; FEMA GRAS; found in almond, asparagus, cocoa, coffee, mushroom, peanut, pork, potato chips, sesame seed, tea; used in sweet sauce, baked goods, candy.

479. 1-PHENYLALANINE - FDA approved food additive; FEMA GRAS; found in meats, eggs, breads, cereals, milk, cheese, fish, corn, beans, potatoes, asparagus, peas; used in frozen dairy, baked goods, candy, condiments, meat products.

480. 3-PHENYLPROPIONALDEHYDE - FDA approved food additive; FEMA GRAS; found in beer, chicken, tomato; used in baked goods, candy, condiments.

481. 3-PHENYLPROPIONIC ACID - FDA approved food additive; FEMA GRAS; found in beef, beer, blue cheese, grape brandy, wheat bread, broccoli, apricot, artichoke, asparagus, banana, beans; used in baked goods, candy.

482. 3-PHENYLPROPYL ACETATE - FDA approved food additive; FEMA GRAS; used in non-alcoholic beverages, ice cream, baked goods, candy, chewing gum, condiments.

483. 3-PHENYLPROPYL CINNAMATE - FDA approved food additive; FEMA GRAS; found in American storax, Peru balsam; used in non-alcoholic beverages, frozen dairy, baked goods, candy, gelatin and puddings.

484. 2-(3-PHENYLPROPYL)TETRAHYDROFURAN - FDA approved food additive; FEMA GRAS; used in baked goods, soft candy, gelatin and puddings, chewing gum.

485. PHOSPHORIC ACID - FEMA GRAS, component of living organisms; used in cheese, baked goods, candy, gelatin and puddings, meat products.

486. PIMENTA LEAF OIL - used in non-alcoholic beverages, ice cream, ices, candy, condiments, chewing gum, meat products.

487. PINE NEEDLE OIL - FDA approved food additive; FEMA GRAS; found in pine tree needles; used in candy, baked goods, ice cream.

488. PINE OIL, SCOTCH - FDA approved food additive; FEMA GRAS; found in pine trees; used in candy, baked goods, non-alcoholic beverages.

489. PINEAPPLE JUICE CONCENTRATE - Found in pineapple; defined as a fruit juice under FDA Standards of Identity

490. alpha-PINENE - FDA approved food additive; FEMA GRAS; found in apple, blueberry, plum brandy, carrots, celery, cheddar cheese, chicken; used in condiments, candy, meat products

491. beta-PINENE - FDA approved food additive; FEMA GRAS; found in apricot, plum brandy, butter, cantaloupe, carrots, celery, cheddar cheese, cocoa, cranberry; used in baked goods, candy, meat products

492. D-PIPERITONE - FDA approved food additive; FEMA GRAS; found in blackberry, celery, raspberry, used in soft candy, baked goods, dairy products.

493. PIPERONAL - FDA GRAS, FEMA GRAS; found in cantaloupe, capers, melon, sherry; used in candy, baked goods.

494. PIPSISSEWA LEAF EXTRACT - FDA GRAS; FEMA GRAS; used in non-alcoholic beverages, candy.

495. PLUM JUICE - Found in plum.

496. POTASSIUM SORBATE - FDA GRAS; FEMA GRAS; found in mountain ash berries; used in cheese.

497. l-PROLINE - FDA approved food additive; FEMA GRAS; essential amino acid, found in proteins, plants and animals; used in breakfast cereals, baked goods.

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498. PROPENYLGUAETHOL - FDA approved food additive; FEMA GRAS; used in sweet sauce, baked goods, candy.

499. PROPIONIC ACID - FDA GRAS; FEMA GRAS; found in apple, apple juice, beef, beer, blueberry juice, bread, cheese, coffee, grape juice, maple syrup, orange juice, raspberry, rum; used in fruit, candy, gelatin and puddings, dairy products.

500. PROPYL ACETATE - FDA approved food additive; FEMA GRAS; found in banana, grape, apple juice, beer, wheat bread, cantaloupe, capers, cocoa, guava, honey, fig, honeydew melon, heated corn oil; used in beverages, ice cream, baked goods.

501. PROPYL para-HYDROXYBENZOATE - FDA approved food additive; FEMA GRAS; found in licorice; used in processed vegetables.

502. PROPYLENE GLYCOL - FDA GRAS; FEMA GRAS; found in sesame seed, mushroom ; used in confection frostings, cheese, candy.

503. 3-PROPYLIDENEPHTHALIDE - FDA approved food addidve; FEMA GRAS; found in lovage; used in frozen dairy products, baked goods, candy.
504. PRUNE JUICE AND CONCENTRATE - Common food item.

505. PYRIDINE - FDA approved food additive; FEMA GRAS; found in bean, bread, cheese, cocoa, coffee, fish, onion, peanut and pecan, popcorn, potato, rum, tea, tomato; used in ice cream, baked goods, condiments, meat products.

506. PYROLIGNEOUS ACID AND EXTRACT - FDA approved food additive; FEMA GRAS; found in Birch tree; used in alcoholic beverages, baked goods, meat products.

507. PYRROLE - FEMA GRAS; found in wheat bread, beer, beef, chicken, steamed clams, cocoa, coffee; used in meat products, candy, baked goods.

508. PYRUVIC ACID - FDA approved food additive; FEMA GRAS; found in beer, wheat bread, celery, asparagus, milk, onion, Sake; used in frozen dairy, products, baked goods, candy.

509. RAISIN JUICE CONCENTRATE - common food item; found in raisin; used in baked goods.

510. RHODINOL - FDA approved food additive; FEMA GRAS; found in geranium flowers; used in chewing gum, baked goods, ice cream.

511. ROSE ABSOLUTE AND OIL - FDA GRAS; FEMA GRAS; found in roses; used in chewing gum, ice cream, baked goods.

512. ROSEMARY OIL - FDA GRAS; FEMA GRAS; found in rosemary; used in condiments, meat products, baked goods.

513. RUM. Alcoholic beverages; natural flavor.

514. RUM ETHER - FDA approved food additive; FEMA GRAS; found in rum; used in non-alcoholic beverages, alcoholic beverages, frozen dairy, baked goods, candy.

515. RYE EXTRACT - found in rye; common food item.

516. SAGE, SAGE OIL, AND SAGE OLEORESIN - FDA GRAS; FEMA GRAS; found in sage; used in baked goods, condiments, meat products.

517. SALICYLALDEHYDE - FDA approved food additive; FEMA GRAS; found in beer, butter, chicken, coffee, cranberry, grape, potato, rum, sherry, tea, tomato, whiskey; used in baked goods, condiments, candy.

518. SANDALWOOD OIL, YELLOW - FDA approved food additive; FEMA GRAS; found in sandalwood; used in candy, baked goods, ice cream.

519. SCLAREOLIDE - FEMA GRAS; found in clary sage; used in milk products, baked goods, candy, meat products, breakfast cereals.

520. SKATOLE - FDA approved food additive; FEMA GRAS; found in cheese, egg, fish, tea; used in frozen dairy, soft candy, gelatin and puddings, baked goods.

521. SMOKE FLAVOR - Found in hickory-wood smoke distillate; used in baked goods, cheese, meats.

522. SNAKEROOT OIL - FDA approved food additive; FEMA GRAS; found in wild ginger; used in beverages, ice cream, candy, condiments.

523. SODIUM ACETATE - FDA GRAS; FEMA GRAS; found in plant and animal tissues; used in cereals, pastas, snack foods, candy, meat products, soups.

524. SODIUM BENZOATE - FDA GRAS; FEMA GRAS; used in baked goods, margarine, dietary supplmements.

525. SODIUM BICARBONATE - FDA GRAS; natural mineral; main component of baking powder and baking soda.

526. SODIUM CARBONATE - FDA GRAS; used in baked goods, desserts, maragarine, poultry.

527. SODIUM CHLORIDE - FDA GRAS; used in brewing, baked goods, butter, cheese, poultry.

528. SODIUM CITRATE - FDA GRAS; FEMA GRAS. used in evaporated milk, general purpose food additive.

529. SODIUM HYDROXIDE - FDA GRAS; Used in meat and poultry, oleo and margarine.

530. SOLANONE - Found in black currant buds

531. SPEARMINT OIL - FDA GRAS; FEMA GRAS. found in spearmint; used in chewing gum, ice cream, candy, baked goods

532. STYRAX EXTRACT, GUM AND OIL - FDA approved food additive; FEMA GRAS; found in storax; used in baked goods, candy, jellies.

533. SUCROSE OCTAACETATE - FDA approved food additive; FEMA GRAS; found in ginger ale; used in candy, gelatin and puddings, baked goods.

534. SUGAR ALCOHOLS - FDA GRAS. FEMA GRAS; found in cherry, plum, apple; used in soft candy. Maltitol is a sugar permitted by FDA for use in chewing gum, diabetic chocolate and whipped non-dairy topping.

535. SUGARS - FDA GRAS; FEMA GRAS. found in food sugar sources; used in baked goods, candy, breakfast cereals.

536. TAGETES OIL - FDA approved food additive; FEMA GRAS; found in marigold flowers; used in condiment relish.

537. TANNIC ACID - FDA GRAS; FEMA GRAS; found in bark of many fruits and plants; used in baked goods, gelatins, puddings and fillings, frozen dairy desserts, candy, meat products.

538. TARTARIC ACID - FDA GRAS; FEMA GRAS; found in wine grapes; used in fruit juices, baked goods, ice cream.

539. TEA LEAF AND ABSOLUTE - FDA GRAS; natural flavor extractive.

540. alpha-TERPINEOL - FDA approved food additive; FEMA GRAS; found in apple, applie juice, apricot, artichoke, beans, beef, beli, bilberry, blueberry, plum brandy; used in chewing gum, baked goods, ice cream.

541. TERPINOLENE - FDA approved food additive; FEMA GRAS; found in thyme, valencia oranges; used in baked goods, ice cream, candy.

542. TERPINYL ACETATE - FDA approved food additive; FEMA GRAS; found in apricot, beer, blackberry, carrots, celery, cranberry, gin, ginger; used in meat products, baked goods, candy.

543. 5,6,7,8-TETRAHYDROQUINOXALINE - FEMA GRAS; found in beef, wheat bread, cocoa, peanut, pork; used in candy, baked goods, dairy products.

544. 1,5,5,9-TETRAMETHYL-13-OXATRICYCLO(8.3.0.0(4,9))TRIDECANE -FEMA GRAS; found in clary sage oil; used in non-alcoholic beverages, ice cream, ices, baked goods, candy, gelatin and puddings.

545. 2,3,4,5 AND 3,4,5,6-TETRAMETHYLETHYL-CYCLOHEXANONE -FDA approved food additive; FEMA GRAS; used in non-alcoholic beverages, ice cream, ices, candy, baked goods.

546. 2,3,5,6-TETRAMETHYLPYRAZINE - FEMA GRAS; found in wheat bread, Sake, shrimp, beef, beer, coffee, peanut; used in baked goods, dairy products, candy.

547. THIAMINE HYDROCHLORIDE - FDA GRAS; FEMA GRAS; found in rice husk, cereal grains, yeast, liver, eggs; nutrient supplement in food.

548. THIAZOLE - FEMA GRAS; found in Coffee aroma, component of the structure of vitamin B1 (Thiamine) which occurs in seeds, meat and milk.

549. l-THREONINE - FDA approved food additive; found in eggs, skim milk, nuts, oranges and lemons.

550. THYME OIL, WHITE AND RED - FDA GRAS; FEMA GRAS; found in thyme; used in condiments, meats, soups, baked goods.

551. THYMOL - FDA approved food additive; FEMA GRAS; found in blueberry, romano sheese, papaya, peppermint, pistacia, fruit tea, wine; used in candy, baked goods, ice cream.

552. TOBACCO EXTRACTS - Natural to tobacco; used as flavorants at minimal levels, producing no measurable increase in nicotine in cigarettes.

553. TOCHOPHEROLS (MIXED) - FDA GRAS; found in spinach, soybeans, cashews; used in pump-cured bacon.

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554. TOLU BALSAM GUM AND EXTRACT - FDA approved food additive; FEMA GRAS; found in balsam tolu; used in baked goods, candy, syrups.

555. TOLUALDEHYDES (ortho,meta,para) - FDA approved food additive; FEMA GRAS; found in beef, beer, butter, coffee, endive, rum, tea; used in chewing gum; baked goods, ice cream.

556. para-TOLYL 3-METHYLBUTYRATE - FEMA GRAS; found in raspberry, coffee, tea, rum; used in baked goods, ice cream, candy.

557. para-TOLYL ACETALDEHYDE - FEMA GRAS; used in ice cream, ices, candy, baked goods.

558. para-TOLYL ACETATE - FDA approved food additive; FEMA GRAS; found in cananga, Ylang Ylang; used in candy, ice cream, baked goods.

559. para-TOLYL ISOBUTYRATE - FDA approved food additive; FEMA GRAS; used in baked goods, ice cream, candy

560. para-TOLYL PHENYLACETATE - FDA approved food additive; FEMA GRAS; used in baked goods, candy, cheese, ice cream.

561. TRIACETIN - FDA GRAS; FEMA GRAS, found in papaya; used in candy, baked goods, ice cream.

562. 2-TRIDECANONE - FEMA GRAS, found in cheese, coffee, coconut oil, hops; used in ice cream, ices, baked goods, candy

563. 2-TRIDECENAL - FDA approved food additive; FEMA GRAS; found in sunguli oil; used in non-alcoholic beverages, ice cream, ices, candy, baked goods, chewing gum.

564. TRIETHYL CITRATE - FDA GRAS; FEMA GRAS; found in red currant; used in chewing gum, baked goods, ice cream.

565. 3,5,5-TRIMETHYL-1-HEXANOL - FEMA GRAS; used in baked goods, condiments, pickles.

566. para,alpha,alpha-TRIMETHYLBENZYL ALCOHOL - FEMA GRAS; found in apricots, blackberry, grape brandy, grapefruit juice, honey, peppermint, pineapple, plum, tomato; used in beverages, candy, gelatins and puddings.

567. 4-(2,6,6-TRIMETHYLCYCLOHEX-1-ENYL)BUT-2-EN-4-ONE - FEMA GRAS; found in rose, rum, brandy, tea; used in baked goods, candy, chewing gum.

568. 2,6,6-TRIMETHYLCYCLOHEX-2-ENE-1,4-DIONE - FEMA GRAS; found in apricot, beer, blackberry, grape, hops, kiwifruit; used in soft candy.

569. 2,6,6-TRIMETHYLCYCLOHEXA-1,3-DIENYL METHAN; FEMA GRAS; used in candy, baked goods, condiments, pickles, preserves and spreads.

570. 4-(2,6,6-TRIMETHYLCYCLOHEXA-1,3-DIENYL)BUT-2-EN-4-ONE; FEMA GRAS; found in apples, black tea, Riesling wine; used in beverages, frozen dessert, baked goods, candy, gelatin and puddings, preserves, condiments.

571. 2,2,6-TRIMETHYLCYCLOHEXANONE - FEMA GRAS; found in bilberry, passion fruit, tea; used in Non-alcoholic beverages, frozen dessert, confectionery, ice cream, ices, candy.

572. 2,3,5-TRIMETHYLPYRAZINE - FEMA GRAS; found in barley, almond, asparagus, beef, wheat bread, chicken, cocoa, coffee; used in baked goods, candy, dairy products, cereals.

573. l-TYROSINE - FDA approved food additive; FEMA GRAS; found in nuts, oranges and lemons.

574. delta-UNDECALACTONE - FEMA GRAS; found in beef, butter, coconut, milk; used in baked goods, candy, dairy products, cereals.

575. gamma-UNDECALACTONE - FDA approved food additive; FEMA GRAS; found in apple, apple juice, apricot, heated butter, peach, plum, pork, rice; used in chewing gum, candy, ice cream, baked goods.

576. UNDECANAL - FDA approved food additive; FEMA GRAS; found in mandarin, grapefruit and lemon; used in baked goods, chewing gum.

577. 2-UNDECANONE - FDA approved food additive; FEMA GRAS; found in coconut oil, banana, beer, beef, cheese, cocoa, coffee, wine, milk, mushroom, peanut, strawberry; used in non-alcoholic beverages, ice cream, baked goods, candy, dairy products.

578. 10-UNDECENAL - FDA approved food additive; FEMA GRAS; used in non-alcoholic beverages, ice cream, ices, candy.

579. UREA - FDA GRAS; found in mushrooms; used in baked goods.

580. VALENCENE - FEMA GRAS; found in grapefruit juice, mango, mangosteen, orange juice, cocoa; used in breakfast cereals, candy, baked goods.

581. VALERALDEHYDE - FDA approved food additive; FEMA GRAS; found in apple, apple juice, apricot, artichoke, asparagus, avocado, banana, beef, blue cheese; used in candy, baked goods, ice cream.

582. VALERIAN ROOT EXTRACT, OIL AND POWDER - FDA approved food additive; FEMA GRAS; found in valerian root; used in baked goods, chewing gum.

583. VALERIC ACID - FDA approved food additive; FEMA GRAS; found in banana, beef, beer, blue cheese, blueberry, wheat bread, butter; used in imitation dairy goods.

584. gamma-VALEROLACTONE - FEMA GRAS; found in beef, beer, cocoa, coffee, mushroom, peach, peanut, wheat bread, heated butter, honey; used in candy, meat products, baked goods.

585. VALINE - FDA approved food additive; FEMA GRAS; found in plants, lemons, oranges, grapefruits; used in ice cream, candy, baked goods.

586. VANILLA EXTRACT AND OLEORESIN - FDA GRAS; FEMA GRAS; found in vanilla bean; used in baked goods, gelatin and puddings, condiments.

587. VANILLIN - FDA GRAS; FEMA GRAS; found in asparagus, barley, beer, brandy, blackberry, blueberry, coffee, cranberry; used in confection frosting, baked goods, candy.

588. VERATRALDEHYDE - FDA approved food additive; FEMA GRAS; found in coffee, raspberry; used in baked goods, ice cream, candy.

589. VETIVER OIL - FDA approved food additive; found in vetiver flowers.

590. VINEGAR - Derived from fermentable sugars such as fruit juices and honey; used in catsup, mayonnaise, pickles.

591. VIOLET LEAF ABSOLUTE - FDA GRAS; FEMA GRAS; found in violets; used in baked goods, ice cream, candy.

592. WALNUT HULL EXTRACT - FDA approved food additive; FEMA GRAS; found in walnuts; used in breakfast cereals, ice cream, candy.

593. WATER.

594. WHEAT EXTRACT AND FLOUR - common food component.

595. WILD CHERRY BARK EXTRACT - FDA GRAS; FEMA GRAS; found in

Cherry trees; used in alcoholic beverages, non-alcoholic beverages, candy, ice cream.

596. WINE AND WINE SHERRY - common beverages, found in grape fermentation/distillation.

597. XANTHAN GUM - FDA approved food additive; produced by carbohydrate fermentation; used in baked goods, beverages, fish, milk, products, poultry.

598. 3,4-XYLENOL - FEMA GRAS; found in coffee, wood vinegar; used in baked goods, meat, soups, coffee, nuts.

599. YEAST - FDA approved food additive

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food technology

JOURNAL OF THE INSTITUTE OF FOOD TECHNOLOGISTS

for

FLAVORING EXTRACT
MANUFACTURERS'
ASSOCIATION

Recent Progress in the Consideration of Flavoring Ingredients Under the Food Additives Amendment

III. GRAS Substances

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FLAVOR EXTRACT MANUFACTURERS' ASSOCIATION
from "Food Technology," Vol. 19, No. 2 (Part 2). Printed in USA by The Garrard Press.

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Recent Progress in the Consideration of Flavoring Ingredients Under the Food Additives Amendment

III. GRAS Substances

RICHARD L. HALL and BERNARD L. OSER

▪ THE Flavoring Extract Manufacturers' Association has conducted a program since 1958 to determine the status of flavoring substances under the Food Additives Amendment of 1958. The key portion of this program has involved the creation of a panel of expert pharmacologists and toxicologists to determine, on the basis of all available data, including experience based on common use in food, what substances are "generally recognized as safe" (GRAS). This article, in a series describing the program, lists all substances which are GRAS and the average maximum use levels at which each has been reported to be used in different categories of food. Inasmuch as all food ingredients, including those that are GRAS, must be used only in accord with good manufacturing practice, certain general guidelines to good manufacturing practice may be drawn from the available data. Such guidelines are presented and discussed.

Previously published articles (Anon., 1961a–f, 1962; Hall, 1959, 1960; Hall and Oser, 1961) and Committee reports (Food Additives Committee, 1958–1964) have given in detail the chronology of the steps taken by the flavoring industry in compliance with the Food Additives Amendment of 1958. The key portion of the program has been the organization of a panel of highly qualified experts who are equipped by both experience and current knowledge to determine general recognition of safety. The background leading to the present article will be found in the list of references, and the article represents the next logical step in the series mentioned above. The data on levels of use which the panel employed in making its judgments are presented in detail for each substance generally recognized as safe. Also stated and discussed are certain general interpretive principles by which these data may be used as guidelines to certain aspects of good manufacturing practice.

COMMON USE FACTOR

The Food Additives Amendment of 1958 states that the term "food additive" means "any substance the intended use of which results . . . directly or indirectly, in its becoming a component . . . of any food . . ., if such substance is not generally recognized, among experts qualified by scientific training and experience to evaluate its safety, as having been adequately shown through scientific procedures (or, in the case of a substance used in food prior to January 1, 1958, through either scientific procedures or *experience based on common use in food*) to be safe under the *conditions of its intended use*; . . ." The phrases from the Food Additives Amendment inextricably couple general recognition of safety with the conditions of intended use. Any adverse indications regarding safety derived from experience in common use may militate against general recognition of safety. Almost all of the flavoring ingredients contained herein were in use prior to January 1, 1958. In almost every case, therefore, common use was a factor, sometimes a major factor, in the panel's final judgment.

The principal source of information on "common use" was a survey of flavoring and representative food manufacturers, conducted by the Flavoring Extract Manufacturers' Association (FEMA). Included in addition to the information derived from this survey are data on chewing gum flavors obtained through the National Association of Chewing Gum Manufacturers, and a limited amount of additional data on candy flavors obtained from several leading manufacturers. While this report does not include all actual flavor uses, it does provide widely representative data from which "common use" can be judged.

It must be emphasized that there can be no general recognition of safety without knowledge of the conditions of intended use and reasonable assurance that actual use conforms appropriately to the intended conditions. This statement applies as fully to those substances which are on the Food and Drug Administration's "White Lists" as to the flavoring ingredients which are on the FEMA GRAS list. This report, therefore, includes both. Those substances which appear only on an FDA White List are indicated in the accompanying survey tabulation with an asterisk.

The enormous variety of flavoring ingredients and the uses to which they may be put make it completely impossible to establish hard-and-fast rules defining their use. As an illustration, oil of clove may be used as a trace ingredient at less than a part per million in the finished food at which level it is not recognizable as such. Or it may be used at a few parts per million as one of the principal flavor notes in a product. Finally, it may reasonably be used at more than 1,000 parts per million when it is the dominant flavor note, for example, in hard candy. Thus in some cases, the use of a substance to impart a dominant note may be at a level more than 1,000 times that of the same substance used as a trace ingredient. In general, the upper limit of use is governed by the general acceptability of the product. Those who have worked with flavors are familiar with this self-limiting characteristic.

A complication which should be noted arises from multiple introductions of a particular chemical entity into a single food product. This occurs because a substance may be added

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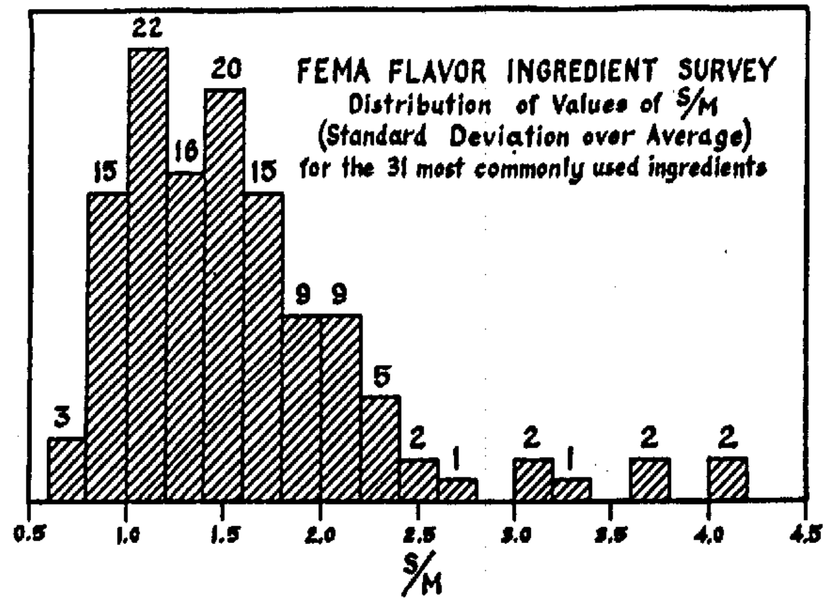

Fig. 1

both as such, and as a normal constituent of one or more natural flavoring materials. For example, the uses reported here of benzaldehyde do not include its use as almond oil added to the same food product, and the uses of eugenol do not reflect that which is separately listed under oil of clove.

GENERAL INTERPRETATIONS

This report reproduces for each major food category on which information was obtained the average of the maximum use levels reported by those firms participating in the survey which appears at the end of this article. The heading "Candy" is taken in the broadest sense, to include chocolate and hard candies such as sour balls, pressed sugar tablets, lozenges, etc. The category "Condiments" includes salad dressings, mustard, relishes, sauces, and comparable highly seasoned food products which are not ordinarily eaten as such but are consumed in conjunction with other foods. The category "Beverages" includes primarily soft drinks, but also some flavored wines and liqueurs which are not specifically listed separately. It also includes beverage tablets and powders, in which cases the use levels involved are computed on the basis of an 8-ounce serving of finished beverage.

In instances where there was only one report, the figure "1" in parentheses appears with the reported maximum use level. Two replies are shown individually rather than as the average.

It is obvious that most averages are derived from sets of figures, some of which may individually depart widely from the mean. Usually, though not necessarily, the average is close to the median, i.e., approximately half of the individual responses will exceed the average, and half be less. One or a few very low or high figures may greatly influence the average. Whether or not this influence by extreme figures is misleading depends on two other factors, neither of which was possible to control. One of these factors is the reliability of the apparently aberrant figure, and the other is the weight which it should be given in the total picture.

A maximum use level that appears to be unreasonably low may show either that the reporting firm used the substance only as a trace ingredient, or that the value may actually have resulted from an error in calculation (e.g., in converting ounces per 100 gallons to parts per million). An extremely high value may represent a reasonable but unusual use, or it, too, could have been erroneous. While an effort was made to recheck extremely high figures, it clearly was not possible, in many cases, to be sure whether the figure represented an error in calculation or an unusual, but nevertheless actual, use.

The second factor concerns the weight that should be given each report. In theory, the averages would be most meaningful if each reply were weighted in proportion to the percentage of total consumption within each food category which that reply covered. In practice, this was impossible to determine, and the only feasible alternative was to use a simple average. This meant, however, that an extreme value could influence the average out of all proportion to its actual importance. This is particularly true of high figures. As every food manufacturer knows, progressively higher flavoring levels (above the most generally preferred or acceptable levels) appeal to progressively smaller segments of the population. Thus, an extremely high use level, even though actual, would ordinarily represent a very limited total consumption. All factors considered, these use figures are reasonably accurate, even though we must remain constantly aware of the qualifications which affect their interpretation.

It should also be noted that the use levels obtained in the survey and reported here are those *introduced* into the food. They do not reflect the losses which may occur in later processing—through volatilization, leaching, or other means.

THE BASIC PROBLEM

We come, then, to the basic problem of how to employ an average maximum use level (bearing in mind the qualifications just stated), as a guide to that "good manufacturing practice" which should govern its "intended use" and is required by both common sense and government regulation. In preparing for this, two steps have been taken:

1) In the calculation of average maximum use levels reported here, responses from the individual manu-

facturer have been omitted which exceed four times the average calculated from data submitted by other firms, provided that these high levels appeared to be separate and distinct from the common levels of use, rather than at the end of a continuous spectrum of values. This was done to eliminate patently erroneous values. In such cases, this obviously resulted in figures lower than the actual arithmetic averages, because (a) unusually low figures were not eliminated, and (b) some isolated high values were undoubtedly real, even though unusual.

2) *All* reports for four principal food categories (beverages, frozen desserts, candy, and baked goods) on the 31 ingredients on which 50 or more replies were received were analyzed statistically. In the analysis of these 124 cases, the elimination procedure described in (1) above was not followed, except for one clearly erroneous value. The average (M) and the standard deviation (S) of the average maximum use levels for each food category were calculated. The data for a possible relationship between M and S were then examined and it was found that one did, indeed, exist, as shown in Fig. 1.

In the most frequent (modal) case, the ratio of the standard deviation to the mean (S/M) ranged between 1.0 and 1.19. In 100 out of 124, S/M was less than 2.00. Careful analysis of those cases where the ratio was 2.0 or greater revealed that either (a) the reported value was obviously in error, or (b) an exceptionally high single flavor note was employed.

Clearly, the great majority of maximum use levels are less than five times the average (M). An even higher proportion of *all* uses (including those less than the maxima) fall below $5M$.

Finally, as mentioned above, extremely high uses strongly influenced S, and to a lesser extent M, in this unweighted average, out of all proportion to the necessarily limited volume of food covered by such high use.

Thus, it is reasonable to conclude that in actual manufacturing practice, a level of five times the average maximum use will include nearly all normal applications of the ingredient.

RATIONALE

This multiple of five is subject to both upward and downward variation in a number of special cases. To define it more usefully and specifically required consideration of a number of determinants, which may operate singly or in combination. The numbered points which follow summarize the effect of these determinants upon use levels, and upon the factor which relates the average maximum level to the general range of good manufacturing practice. A brief discussion of the rationale is included where appropriate.

1) If a flavoring substance is used to provide the principal, or a single, flavoring note, the level of use may be more than five times the average maximum use level.

2) While there are many exceptions, natural flavors are, in general, used at higher levels than synthetic components. In the 124 cases analyzed, only 15 concern an average maximum use in excess of 500 ppm in any single food category. Thirteen of these cases involve natural oils or extracts (Table 1).

Table 1. Cases in which the average maximum use level is greater than 500 ppm.

Substance	Recalculated av. max. use level (ppm)[a]	S/M	Food category
Anise, oil	570.	1.82	Candy
Cassia bark, oil	750.	.78	Candy
Cinnamaldehyde	670.	1.72	Candy
Grapefruit, oil	570.	1.16	Candy
Lemon, oil	1,000.	1.04	Candy
	540.	.90	Baked goods
Lime, oil	700.	1.00	Candy
Methyl salicylate	930.	2.29	Candy
Orange peel, sweet, oil	1,200.	1.22	Candy
	550.	.92	Baked goods
Peppermint, oil	1,200.	1.17	Candy
Vanilla, extract	1,800.	1.48	Beverages
	2,900.	1.16	Ice cream, ices, etc.
	2,700.	1.09	Candy
	4,100.	1.68	Baked goods

[a] These are recalculated, including *all* data (see text).

3) Substances used at very high levels usually entail a smaller multiple of the average maximum than those used at lower levels. In the 15 cases (Table 1) where the levels of use are more than 500 ppm, only one, methyl salicylate, involves an S/M value higher than 1.82. The use of methyl salicylate in hard candy and chewing gum presents some unusual aspects, of which this is one. Ten of the fifteen cases are below 1.23. Thus, most would be covered by a factor of $3M$, rather than $5M$. On the other hand, all of the 22 cases in Table 2 in which S/M is greater than two, and thus not covered by $5M$, are concerned with uses under 200 ppm, again except for methyl salicylate. In two instances, S/M is exactly 2.0. All but six of these 24 cases are below 120 ppm.

Table 2. Cases in which S/M is 2.0 or greater.

Substance	Recalculated av. max. use level (ppm)[a]	S/M	Food category
Acetic acid	110.	2.16	Ice cream, ices, etc.
Anise, oil	50.	4.19	Beverages
Benzaldehyde	96.	3.1	Beverages
	120.	3.1	Ice cream, ices, etc.
Butyric acid	26.	2.02	Beverages
	84.	2.1	Baked goods
Cassia bark, oil	49.	2.32	Beverages
	100.	2.55	Ice cream, ices, etc.
Clove bud, oil	14.	2.00	Beverages
Coriander, oil	78.	2.6	Candy
	67.	2.6	Baked goods
	66.	4.0	Ice cream, ices, etc.
Diacetyl	3.7	2.00	Beverages
Ethyl butyrate	40.	2.15	Beverages
	36.	2.23	Ice cream, ices, etc.
Ethyl methyl phenylglycidate	16.	2.23	Ice cream, ices, etc.
Ethyl vanillin	170.	2.30	Candy
	170.	2.60	Baked goods
Lemon oil, terpeneless	39.	2.47	Beverages
	93.	2.23	Ice cream, ices, etc.
	100.	2.17	Candy
	120.	2.56	Baked goods
Methyl salicylate	930.	2.29	Candy
Nutmeg, oil	200.	2.04	Baked goods

[a] These are recalculated, including *all* data (see text).

4) Products such as hard candies and some baked or fried goods involve processing with resultant high flavor losses. This requires the flavor to be introduced at high levels, and may involve a wider range than in other foods, such as beverages, in which no processing losses occur. Of the 15 high-level cases (average maximum use level greater than 500 ppm) in Table 1, 13 deal with baked goods and candies. The other two are vanilla extract in beverages and ice cream. Vanilla extract is ordinarily used at a relatively high level in any food product.

5) Of the 22 cases involving S/M ratios greater than 2.0, most are

explainable by the foregoing causes. In addition, it must be pointed out that foods consumed in small portions tend to be flavored at high levels. Obvious examples are chewing gum, flavored wines, liqueurs, and hard candies. The special considerations applicable to chewing gum are discussed in considerable detail by Heggie *et al.* (1965). The FEMA survey reflects primarily soft-candy uses, since hard candies (including lozenges and pressed mints) are only approximately 12.5 percent of total U. S. candy production (Steinberg, 1963). It was evident from the data that the "average maxima" of hard-candy uses ran from 2 to 10 times the average maximum use levels reported for all candy in the survey reported here, and on rare occasions were higher.

One may estimate the confidence which can be placed in the reported average maximum-use levels from the total number of replies on which these figures are based. This is given in the first column to the right of the name of the substance. Obviously, for substances on which a large number of responses were received, the average figure is more reliable than in cases where only a handful of reports were received.

These considerations, applied to the average maximum-use levels, are consistent with good manufacturing practice, and were taken into account by the panel in arriving at its judgments that these substances are generally recognized as safe. The panel's conclusions were based on over-all conditions of use of each substance in relation to its total intake.

GUIDELINES, NOT TOLERANCES

The Food and Drug Administration has constantly emphasized the necessity of observing "good manufacturing practice." In Paragraph 121.101, it defines the term to include the following restrictions:

"(1) The quantity of the substance added to food does not exceed the amount reasonably required to accomplish its intended physical, nutritive, or other technical effect in food.

"(2) Any substance intended for use in or on food is of appropriate food grade and is prepared and handled as a food ingredient."

The figures presented and discussed in this report are not tolerances. The word "tolerance" means a level within the safe range established by scientific procedures, but no greater than necessary to achieve the desired effect, and hence above which the substance may not legally be used. In contrast, the figures cited here are averages to which certain flexible principles, stated above, must be applied. It is the opinion of the expert panel that, except where specifically noted, it is neither necessary nor practical to establish tolerances or rigid use limits for the flavoring substances covered by this report.

It is clear that the fact that a flavor ingredient may have been reported as used only in certain food categories does not necessarily preclude its use, as a substance generally recognized as safe, in other categories within the principles stated above. However, in special cases where flavoring substances are used in a manner, or at levels, substantially different from those embraced by current good manufacturing practice, justification for such uses, in terms of safety and necessity, may have to be accomplished independently by the user concerned.

It is again emphasized that these are guidelines to "good manufacturing practice" or to "intended use" or to "common use" in which these substances are generally recognized as safe. They are not tolerances in any sense of the word.

ACKNOWLEDGMENTS

It should be noted that the work reported here is the result of the contributions of many individuals. Special thanks go to the members of the Food Additives Committee of the FEMA, and to the expert panel, not merely for time and professional effort expended but for the active personal interest unstintingly displayed. Acknowledgment is also made to Miss Janis Klima, for invaluable contributions to organizing, recording, and reporting the work, and to Mr. John Thomas Johnson, of Loyola College, Baltimore, Maryland, for helpful advice and assistance in statistical analysis of the data.

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SURVEY OF FLAVORING INGREDIENT USAGE LEVELS

Flavoring Extract Manufacturers' Association average maximum use levels (in ppm) on which the expert panel based its judgments that the substances are generally recognized as safe. Those substances which appear only on an FDA "White List" are indicated with an asterisk.

FEMA No. and Substance	No. of Reports	Beverages	Ice Cream, Ices, Etc.	Candy	Baked Goods	Gelatins and Puddings	Chewing Gum	— Other Category Uses —		
2001 *ACACIA, GUM (*Acacia senegal* (L.) Willd.)--Arabic, gum	102	330.	430.	410.	460.	840.	740. 2,800.	*Meringue* 750. 7,000.	*Syrups* 210. 240.	
2002 ACETAL--Acetaldehyde diethyl acetal	7	7.3	52.	39.	6.0 120.					
2003 ACETALDEHYDE--Ethanal	33	3.9	25.	22.	12.	6.8	20. 270.			
2004 ACETALDEHYDE PHENETHYL PROPYL ACETAL--Acetal R, Pepital	1	-	-	(1)2.5	(1)2.5					
2005 ACETANISOLE--4'-Methoxyacetophenone; p-Acetyl anisole, p-Methoxyacetophenone; Novatone	12	2.3	2.5	4.6	5.8		(1)840.			
2006 ACETIC ACID--Ethanoic acid	60	39.	32.	52.	38.	(1)15.	60. 60.	*Condiments* 5,900.		
2007 (tri-)ACETIN--Glyceryl triacetate; Enzactin; Vanay	9	190.	60. 2,000.	560.	1,000.		(1)4,100.			
2008 ACETOIN--3-Hydroxy-2-butanone, Acetyl methyl carbinol, 2,3-Butanolone; Y-Hydroxy-β-oxobutane; Dimethylketol	34	7.4	3.3	18.	32.	0.60 21.		*Cottage Cheese* (1)7.0	*Margarine* 0.80 50.	*Shortening* (1)8.0
2009 ACETOPHENONE--Methyl phenyl ketone; Acetyl benzene, Hypnone	24	0.98	2.8	3.6	5.6	(1)7.0	0.60 20.			
2010 ACONITIC ACID--1-Propene-1,2,3-tricarboxylic acid, Achilleic acid; Citridic acid; Equisetic acid	4	0.20 2.0	(1)0.60	0.60 30.	0.60 15.		(1)28.	*Alcoholic Beverages* (1)20.		
2011 ADIPIC ACID--1,4-Butanedicarboxylic acid; Hexanedioic acid	2	(1)40.	-	-	-	(1)5,000.				
2012 *AGAR--*Gelidium cartilagineum* (L.) Gaillon and *Gracilaria confervoides* (L.) Greville and related red algae	10	420. 1,000.	130. 1,000.	-	490.			*Icings* 300. 30,000.	*Meringue* (1)2,000.	
2013 *ALFALFA, EXTRACT--*Medicago sativa* L.	2	(1)10.	-	-	-			*Alcoholic Beverages* (1)200.		
2014 *ALGIN--*Laminaria* spp. and other kelps	9	100. 240.	2,000. 2,400.	-	-	(1)4,000.		*Emulsions* (1)100.		
2015 ALGINATES, SODIUM, CALCIUM, and AMMONIUM	25	340.	1,000.	-	70. 200.			*Condiments* 5,200.	*Meats* (1)1,000.	*Toppings* 4,500.
2016 ALKANET ROOT, EXTRACT (*Alkanna tinctoria* Tausch)--Alcannin, extract; Alkannin, extract; Anchusin, extract	6	(1)1.0	(1)3.0	(1)10.	(1)10.			*Icings* (1)70.	*Meats* (1)0.20	
2017 *ALLSPICE--*Pimenta officinalis* Lindl.	36	120.	1.5 2.0	(1)2.0	1,400.		(1)40.	*Condiments* 1,000.	*Meats* 670.	
2018 *ALLSPICE, OIL--*Pimenta officinalis* Lindl.	56	18.	15.	66.	48.		40. 1,700.	*Alcoholic Beverages* (1)5.0 *Meats* 110.	*Condiments* 70. *Pickles* 29.	*Soups* (1)55.
2019 *ALLSPICE, OLEORESIN--*Pimenta officinalis* Lindl.	8	-	-	-	(1)600.			*Condiments* 25. 130.	*Meats* 69.	
2020 ALLYL ANTHRANILATE	5	1.1	0.67	2.0	0.02 1.0	(1)2.0				
2021 ALLYL BUTYRATE	6	1.2	0.50 1.0	1.3	0.50 3.0	(1)1.0				
2022 ALLYL CINNAMATE	8	1.0	1.4	1.8	2.6					
2023 ALLYL CYCLOHEXANEACETATE	5	1.1	1.6	3.5	4.0					

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FEMA No. and Substance	No. of Reports	Beverages	Ice Cream, Ices, Etc.	Candy	Baked Goods	Gelatins and Puddings	Chewing Gum	— Other Category Uses —		
2024 ALLYL CYCLOHEXANEBUTYRATE	6	1.0	1.4	3.3	3.8					
2025 ALLYL CYCLOHEXANEHEXANOATE	3	(1)1.4	(1)3.3	8.0	8.5					
2026 ALLYL CYCLOHEXANEPROPIONATE--Allyl 3-cyclohexylpropionate; Allyl-β-cyclohexylpropionate	30	3.7	3.1	13.	7.1	7.7	(1)30.	*Icings* (1)0.20		
2027 ALLYL CYCLOHEXANEVALERATE	5	1.2	2.3	4.4	4.8					
2028 ALLYL DISULFIDE--Diallyl disulfide	5	.	.	.	.			*Condiments* 6.5	*Meats* 7.0	
2029 ALLYL 2-ETHYLBUTYRATE	2	0.50 1.0	.	(1)2.0	.	(1)1.0				
2030 ALLYL 2-FUROATE	5	0.53	0.05 2.0	1.6	0.75 2.0	(1)1.0				
2031 ALLYL HEPTANOATE--Allyl enanthate; Allyl heptoate; Allyl heptylate	15	1.3	2.7	6.4	6.4	2.9	(1)86.			
2032 ALLYL HEXANOATE--2-Propenyl hexanoate	52	7.0	11.	32.	25.	22.	210.			
2033 ALLYL α-IONONE--1-(2,6,6-Trimethyl-2-cyclohexene-1-yl)-1,6-heptadien-3-one; Cetone V	6	0.50	1.4	2.6	3.1	(1)1.0		*Toppings* (1)2.0		
2034 ALLYL ISOTHIOCYANATE--Mustard oil	23	0.02 0.50	(1)0.50	(1)0.50	5.2			*Condiments* 52.	*Meats* 87.	*Pickles* 10. 88.
2035 ALLYL MERCAPTAN--2-Propene-1-thiol; Allylthiol; Allyl sulfhydrate	4	(1)0.25	0.50 2.0	(1)0.50	0.60 2.0			*Condiments* 2.0 3.0	*Meats* (1)0.50	
2036 ALLYL NONANOATE	4	0.70	0.50 3.0	5.0	3.0 5.0				*Meats* (1)1.0	
2037 ALLYL OCTANOATE	15	1.7	3.3	5.1	4.0	(1)0.10				
2038 ALLYL PHENOXYACETATE--Acetate PA	4	0.82	0.004 0.40	2.3	0.03 1.0	(1)3.0				
2039 ALLYL PHENYLACETATE	3	0.06 3.0	(1)8.0	14.	(1)40.					
2040 ALLYL PROPIONATE	3	0.06 3.0	(1)16.	6.8	(1)10.					
2041 ALLYL SORBATE--2,4-Hexadienoate	3	0.86	(1)0.30	0.50 5.0	(1)1.0	(1)2.0				
2042 ALLYL SULFIDE--Thioallyl ether; Diallyl sulfide	10	0.04	0.06	0.07	0.05			*Condiments* 13.	*Meats* 3.7	
2043 ALLYL TIGLATE--Allyl *trans*-2-methyl-2-butenoate	3	0.28	0.50 0.50	0.50 3.0	0.50 3.0					
2044 ALLYL 10-UNDECENOATE--Allyl undecylenate	2	0.25 1.0	0.50 0.50	(1)0.50	(1)0.50					
2045 ALLYL *iso*-VALERATE	5	8.6	18.	22.	15. 48.	(1)1.0				
2046 *ALMONDS, BITTER, OIL (FFPA)--*Prunus amygdalus* Batsch var. *amara* (DC.) Focke	99	80.	66.	97.	96.	29.	330.	*Maraschino Cherries* 340.		
2047 ALOE, EXTRACT--*Aloe* spp.	4	5.0 2,000.	.	.	.			*Alcoholic Beverages* (1)130.		
2048 ALTHEA ROOT [*Althea officinalis* L.]--Marshmallow root	3	5.7 10.	.	.	.					
2049 *AMBERGRIS, TINCTURE	4	2.0	1.7	9.7	(1)0.10					
2050 *AMBRETTE, ABSOLUTE, OIL--*Hibiscus abelmoschus* L.	3	0.14	0.22	0.34	0.34					
2051 *AMBRETTE SEED, OIL--*Hibiscus abelmoschus* L.	3	0.30	0.30 0.50	0.80	0.80					
2052 *AMBRETTE, TINCTURE--*Hibiscus abelmoschus* L.	3	(1)5.0	1.0 5.0	0.04 10.	(1)10.			*Alcoholic Beverages* (1)10.		

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FEMA No. and Substance	No. of Reports	Beverages	Ice Cream, Ices, Etc.	Candy	Baked Goods	Gelatins and Puddings	Chewing Gum	— Other Category Uses —
2053 AMMONIUM SULFIDE	1	-	-	-	(1)5.0			*Condiments* (1)5.0
2054 AMMONIUM *iso*-VALERATE	4	-	-	-	58.			*Syrups* (1)0.20
2055 *iso*-AMYL ACETATE * --common Amyl acetate; β-Methyl butyl acetate	72	28.	56.	190.	120.	100.	2,700.	
2056 AMYL ALCOHOL--Pentyl alcohol; 1-Pentanol	16	18.	23.	35.	24.	7.7 50.	150. 340.	
2057 *iso*-AMYL ALCOHOL--*iso*-Pentyl alcohol; 3-Methyl-1-butanol; *iso*-Butyl carbinol	21	17.	7.6	52.	24.	46.	(1)300.	*Alcoholic Beverages* (1)100.
2058 *iso*-AMYL BENZOATE--*iso*-Pentyl benzoate	13	3.0	2.5	3.5	7.4	(1)4.6	(1)200.	
2059 AMYL BUTYRATE--Pentyl butyrate	45	19.	32.	76.	43.	0.50 1.4	760.	*Syrups* (1)58.
2060 *iso*-AMYL BUTYRATE--*iso*-Pentyl butyrate	37	13.	34.	79.	51.	60.	570.	
2061 α-AMYLCINNAMALDEHYDE--α-Pentylcinnamaldehyde; α-Amyl β-phenylacrolein, Buxine®	20	1.3	1.5	4.0	4.5	0.03 0.05	(1)15.	
2062 α-AMYLCINNAMALDEHYDE DIMETHYL ACETAL--1.1-Dimethoxy-2-amyl-3-phenyl-2-propene	5	0.80	1.5 3.0	(1)2.0	2.6			
2063 *iso*-AMYL CINNAMATE--*iso*-Pentyl cinnamate	13	3.1	4.2	13.	13.			
2064 α-AMYLCINNAMYL ACETATE--α-Pentylcinnamyl acetate	4	0.92	3.5	3.5	3.0		(1)3.0	
2065 α-AMYLCINNAMYL ALCOHOL--α-Pentylcinnamyl alcohol	6	0.47	1.5	1.6	1.5		(1)2.0	
2066 α-AMYLCINNAMYL FORMATE--α-Pentylcinnamyl formate	3	0.17	0.93	1.5	1.5		(1)1.0	
2067 α-AMYLCINNAMYL *iso*-VALERATE--α-Pentylcinnamyl *iso*-valerate	4	0.36	1.2	1.3	1.7		(1)1.0	
2068 AMYL FORMATE--Pentyl formate	22	13.	21.	31.	8.0		170.	
2069 *iso*-AMYL FORMATE--*iso*-Pentyl formate	23	8.4	24.	22.	16.	2.0 28.	250.	
2070 *iso*-AMYL 2-FURANBUTYRATE--*iso*-Pentyl 2-furanbutyrate; α-*iso*-Amyl furfurylpropionate	5	0.03 5.0	12.8	6.0	0.50 8.0	(1)5.0		
2071 *iso*-AMYL 2-FURANPROPIONATE--*iso*-Pentyl 2-furanpropionate; α-*iso*-Amyl furfurylacetate	4	0.02 0.33	0.33 0.65	1.6 3.6	1.6 3.6			
2072 AMYL 2-FUROATE--Pentyl 2-furoate	3	(1)5.0	-	1.5 6.0	(1)1.0			*Condiments* (1)10.
2073 AMYL HEPTANOATE--Pentyl heptanoate	9	7.0	3.8	7.5	3.0	(1)3.5	(1)53.	
2074 AMYL HEXANOATE--Pentyl hexanoate	16	5.3	16.	22.	8.3	0.30 3.7	(1)110.	
2075 *iso*-AMYL HEXANOATE--*iso*-Pentyl hexanoate	19	7.8	14.	17.	15.	(1)3.7		
2076 2-AMYL-5 or 6-KETO-1,4-DIOXANE	1		8.0	(1)5.0	(1)5.0			*Shortening* (1)5.0
2077 *iso*-AMYL LAURATE--*iso*-Pentyl laurate; *iso*-Amyl dodecanoate	2	0.04 3.0	0.16 6.0	0.50 6.0	0.50 6.0			
2078 *iso*-AMYL NONANOATE--*iso*-Pentyl nonanoate	6	1.5	3.3	3.0	4.0			
2079 AMYL OCTANOATE--Pentyl octanoate	8	5.0	3.5	6.0	3.5	(1)2.1		
2080 *iso*-AMYL OCTANOATE--*iso*-Pentyl octanoate	10	6.6	5.1	7.4	3.5	(1)2.1		

* Throughout this report, the names "*iso*-amyl" and "amyl" are used in accord with the rules of chemical nomenclature. In commercial practice, however, "amyl" invariably means "*iso*-amyl" unless it is prefaced by the *n*- for normal.

FEMA No. and Substance	No. of Reports	Beverages	Ice Cream, Ices, Etc.	Candy	Baked Goods	Gelatins and Puddings	Chewing Gum	— Other Category Uses —		
2081 iso-AMYL PHENYLACETATE--*iso*-Pentyl phenylacetate	22	5.0	16.	12.	14.	0.15 3.4		*Toppings* 0.25 0.80		
2082 iso-AMYL PROPIONATE--*iso*-Pentyl propionate	14	3.8	13.	38.	6.1	0.80 3.7	750.			
2083 iso-AMYL PYRUVATE--*iso*-Pentyl pyruvate	4	4.7	8.1	9.2	12.					
2084 iso-AMYL SALICYLATE--*iso*-Pentyl salicylate; *iso*-Amyl o-hydroxybenzoate, Orchidee	6	1.4	2.9	3.0	3.0					
2085 iso-AMYL *iso*-VALERATE--*iso*-Pentyl *iso*-valerate	35	8.5	14.	33.	41.	1.0 61.	390.	*Jellies* (1)10.		
2086 ANETHOLE--*p*-Propenylanisole, 1-Methoxy-4-propenylbenzene; Anise camphor	43	11.	26.	340.	150.		1,500.	*Alcoholic Beverages* 1,400.		
2087 *ANGELICA ROOT, EXTRACT--*Angelica archangelica* L.	12	49.	46.	44.	61.			*Syrups* 1.0 100.		
2088 *ANGELICA ROOT, OIL--*Angelica archangelica* L.	18	12.	0.99	0.86	1.0	0.03 5.0	(1)60.	*Alcoholic Beverages* 15.		
2089 *ANGELICA SEED, EXTRACT--*Angelica archangelica* L.	6	1,100.	-	19.	(1)50.			*Condiments* (1)10.	*Syrups* (1)100.	
2090 *ANGELICA SEED, OIL--*Angelica archangelica* L.	10	6.3	1.4	1.9	2.2	(1)5.0		*Alcoholic Beverages* 32.		
2091 *ANGELICA STEM, OIL--*Angelica archangelica* L.	2	0.50 1.5	0.50 10.	1.0 25.	1.0 24.	(1)0.50				
2092 *ANGOSTURA, EXTRACT--*Galipea officinalis* Hancock	8	18.	-	-	-			*Alcoholic Beverages* 1,700.		
2093 *ANISE--*Pimpinella anisum* L.	17	2.0 30.	1.0 4.0	3.0 4.0	490.			*Condiments* 55. 5,000.	*Meats* 1,200.	
2094 *ANISE, OIL--*Pimpinella anisum* L.	83	7.5	67.	500.	120.		3,200.	*Alcoholic Beverages* 45.	*Meats* 65.	
2095 *ANISE, STAR--*Illicium verum* Hook. f.	33	13.	18.	83.	140.			*Alcoholic Beverages* 40. 60.	*Meats* 500. 1,000.	
2096 ANISE, STAR, OIL--*Illicium verum* Hook. f.	46	12.	99.	190.	230.			*Alcoholic Beverages* 50.	*Meats* 20. 55.	*Syrups* (1)8.0
2097 ANISOLE--Methoxybenzene; Methylphenyl ether	6	9.0	16.	51.	34.					
2098 ANISYL ACETATE--*p*-Methoxybenzyl acetate	21	6.3	8.0	15.	12.	11.	(1)30.			
2099 ANISYL ALCOHOL--*p*-Methoxybenzyl alcohol; Anisic alcohol	15	7.4	8.0	11.	12.	(1)1.9				
2100 ANISYL BUTYRATE--*p*-Methoxybenzyl butyrate	4	3.1	5.7	10.	13.					
2101 ANISYL FORMATE--*p*-Methoxybenzyl formate	9	3.2	3.9	7.9	14.	(1)0.20				
2102 ANISYL PROPIONATE--*p*-Methoxybenzyl propionate	14	5.6	6.1	16.	20.	(1)0.25				
2103 ANNATTO, EXTRACT [*Bixa orellana* L.]--Arnotta, extract; Annotta, extract	14	(1)25.	200.	-	2,000.			*Breakfast Cereals* (1)2,000.	*Margarine* 330.	
2104 ANNATTO, SEED [*Bixa orellana* L.]--Arnotta, seed; Annotta, seed	3	-	-	-	100. 100.					
2105 *APRICOT KERNEL, OIL [*Prunus armeniaca* L.]--Persic, oil	9	130. 150.	3.4 400.	300. 360.	270.			*Soups* 1.0 500.		
2106 *ASAFETIDA, FLUID EXTRACT--*Ferula assa-foetida* L.	4	(1)4.0	(1)10.	(1)5.0	8.0 10.			*Condiments* (1)50.	*Meats* (1)10.	*Soups* (1)30.
2107 *ASAFETIDA, GUM--*Ferula assa-foetida* L.	5	(1)5.0	(1)10.	15. 25.	(1)15.			*Condiments* 5.0 160.		

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FEMA No. and Substance	No. of Reports	Beverages	Ice Cream, Ices, Etc.	Candy	Baked Goods	Gelatins and Puddings	Chewing Gum	— Other Category Uses —	
2108 *ASAFETIDA, OIL—*Ferula assa-foetida* L.	3	-	-	1.0 15.	(1)1.0			*Condiments* (1)10.	
2109 ASCORBIC ACID—Vitamin C	34	130.	0.80 250.	4.0 6,000.	1.0 500.			*Fruit Sauces* 280. 380.	*Meats* 0.49 470.
2110 *ASH BARK, PRICKLY, EXTRACT—*Xanthoxylum americanum* L. or *Xanthoxylum clava-herculis* L.	4	59.	-	(1)78.	(1)82.				
2111 *BALM [*Melissa officinalis* L.]—Balm, lemon	0	-	-	-	-				
2112 *BALM LEAVES, EXTRACT [*Melissa officinalis* L.]—Balm, lemon, extract; Melissa, extract	1	(1)2,000.	-	-	-				
2113 *BALM, OIL [*Melissa officinalis* L.]—Balm, lemon, oil; Melissa, oil	7	8.5	1.7 15.	20.	10. 60.				
2114 BALSAM FIR, OIL—*Abies balsamea* (L.) Mill.	7	4.5	0.50 1.5	5.2	5.2	0.50 1.0			
2115 BALSAM FIR, OLEORESIN—*Abies balsamea* (L.) Mill.	3	(1)0.20	(1)1.5	(1)5.0	(1)5.0				
2116 *BALSAM, PERU—*Myroxylon pereirae* Klotzsch	38	3.0	5.9	10.	32.	0.05 1.0	120.	*Syrups* -0.25 7.0	
2117 *BALSAM, PERU, OIL—*Myroxylon pereirae* Klotzsch	15	3.2	2.2	8.4	6.6				
2118 *BASIL—*Ocimum basilicum* L.	20	(1)2.5	(1)5.0	(1)5.0	680.			*Condiments* 500.	*Meats* 520.
2119 *BASIL, OIL—*Ocimum basilicum* L.	21	2.0	2.7	6.2	4.2	(1)0.01		*Condiments* 15.	*Meats* 24.
2120 *BASIL, OLEORESIN—*Ocimum basilicum* L.	3	-	-	-	(1)16.			*Condiments* 2.0 5.0	
2121 *BAY LEAVES, WEST INDIAN, EXTRACT—*Pimenta acris* Kostel	8	0.67	(1)2.0	1.6 2.0	(1)2.0			*Meats* 54.	*Soups* (1)0.72
2122 *BAY LEAVES, WEST INDIAN, OIL [*Pimenta acris* Kostel]—Myrcia, oil	16	1.5	2.3	4.4	4.6			*Condiments* 27.	*Meats* 15.
2123 *BAY LEAVES, WEST INDIAN, OLEORESIN—*Pimenta acris* Kostel	3	-	-	-	-			*Meats* 25. 25.	*Soups* (1)72.
2124 *BAY, SWEET—*Laurus nobilis* L.	18	0.36 2.5	(1)5.0	(1)5.0	5.0 400.			*Condiments* 130.	*Meats* 840.
2125 *BAY, SWEET, OIL—*Laurus nobilis* L.	6	2.0	1.8	2.6	21.		(1)2.9	*Condiments* (1)30.	
2126 BEESWAX, WHITE [*Apis mellifera* L.]—Cire d'abeille absolute	5	0.50 0.50	2.0	10.	10.			*Honey* (1)5.0	
2127 BENZALDEHYDE—Benzenecarbonal; Benzenemethylal; Benzoic aldehyde	78	36.	42.	120.	110.	160.	840.	*Alcoholic Beverages* 50. 60.	
2128 BENZALDEHYDE DIMETHYL ACETAL	5	26.	22.	56.	45.	(1)50.		*Alcoholic Beverages* (1)60.	
2129 BENZALDEHYDE GLYCERYL ACETAL—2-Phenyl-m-dioxan-5-ol	9	21.	24.	110.	73.	100.	(1)840.		
2130 BENZALDEHYDE PROPYLENE GLYCOL ACETAL—4-Methyl-2-phenyl-m-dioxolane	5	34.	27.	110.	96.	(1)50.			
2131 BENZOIC ACID—Benzenecarboxylic acid; Phenylformic acid; Dracylic acid	14	7.5	4.8	8.9	40.		20. 32.	*Icings* (1)250.	
2132 BENZOIN—2-Hydroxy-2-phenylacetophenone	3	4.5	0.54	2.0	1.4	(1)0.10			
2133 BENZOIN, RESIN [*Styrax benzoin* Dryander; *S. paralleloneurus* Perkins; *S. tonkinensis* (Pierre) Craib ex Hartwich, or other spp. of the Section *Anthostyrax* of the genus *Styrax*]—Gum Benjamin; Benzoe	16	15.	5.1	8.7	26.	(1)10.	(1)110.		

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FEMA No. and Substance	No. of Reports	Beverages	Ice Cream, Ices, Etc.	Candy	Baked Goods	Gelatins and Puddings	Chewing Gum	— Other Category Uses —
2134 BENZOPHENONE--Diphenyl ketone; Benzoyl-benzene	8	0.50	0.61	1.7	2.4			
2135 BENZYL ACETATE	38	7.8	14.	34.	22.	23.	760.	
2136 BENZYL ACETOACETATE--Benzyl acetyl acetate	5	2.7	6.0	13.	13.	0.50 10.	(1)50.	
2137 BENZYL ALCOHOL--Phenyl carbinol; Phenyl methanol; α-Hydroxytoluene	24	15.	160.	47.	220.	21. 45.	1,200.	
2138 BENZYL BENZOATE--Benzyl benzene carboxylate; Benzyl phenylformate	20	4.5	12.	39.	33.		280.	
2139 BENZYL BUTYL ETHER	2	0.50 2.0	(1)3.5	(1)8.0	2.0 8.0	(1)2.0		
2140 BENZYL BUTYRATE--Benzyl butanoate	24	4.5	6.9	7.7	9.9	(1)3.0	(1)310.	
2141 BENZYL *iso*-BUTYRATE--Benzyl 2-methyl propanoate	11	5.2	12.	12.	25.			
2142 BENZYL CINNAMATE--Benzyl β-Phenylacrylate; Cinnamein	20	1.4	2.5	6.7	6.6	3.0 5.0	5.3 120.	
2143 BENZYL 2,3-DIMETHYLCROTONATE--Benzyl methyl tiglate	4	0.75	2.8	1.8	1.5			
2144 BENZYL ETHYL ETHER	2	0.50 1.0	(1)2.5	(1)7.5	(1)7.5			
2145 BENZYL FORMATE	14	2.4	8.0	12.	8.6		(1)3.2	
2146 3-BENZYL-4-HEPTANONE--Benzyl dipropyl ketone; Morellone	4	1.2	4.6	11.	11.			
2147 BENZYL MERCAPTAN--α-Toluenethiol; Benzylthiol	2	0.15 0.25	0.15 0.50	0.50 0.75	0.50 0.75			
2148 BENZYL METHOXYETHYL ACETAL--Acetaldehyde benzyl β-methoxyethyl acetal; 1-Benzyloxy-1-(β-methoxy)ethoxy ethane	1	(1)0.50	(1)1.0	(1)1.0	(1)1.0			
2149 BENZYL PHENYLACETATE	9	1.3	2.6	6.6	4.3			*Toppings* (1)6.0
2150 BENZYL PROPIONATE--Benzyl propanoate	20	4.1	5.8	19.	17.		19. 150.	*Icings* (1)40.
2151 BENZYL SALICYLATE--Benzyl o-hydroxybenzoate	7	1.4	0.89	1.8	0.01 2.2			
2152 BENZYL *iso*-VALERATE	16	2.2	3.4	16.	9.4	(1)56.	(1)200.	
2153 *BERGAMOT, OIL [*Citrus aurantium* L. subsp. *bergamia* Wright et Arn.]--Bergamot orange, oil	29	8.9	7.9	27.	29.	5.3 90.	43.	*Icings* 1.0 130.
2154 BIRCH, SWEET, OIL [*Betula lenta* L.]--Birch, black, oil	97	48.	44.	310.	110.	(1)0.07	4,300.	*Syrups* (1)5.0
2155 BLACKBERRY BARK, EXTRACT--*Rubus*, spp. of Section *Eubatus*	7	81.	3.0 880.	230.	3.0 660.			*Alcoholic Beverages* 150. 10,000.
2156 *BOIS DE ROSE, OIL--*Aniba rosaeodora* Ducke	12	0.65	2.6	6.7	9.3		(1)35.	
2157 BORNEOL--Bornyl alcohol, 2-Hydroxycamphane; Borneocamphor, 2-Camphanol; *d*-Camphanol	8	0.25 1.4	(1)1.4	3.7	5.1		(1)0.30	*Syrups* (1)0.30
2158 *iso*-BORNEOL	4	6.2	23.	11.	8.3		(1)0.80	
2159 BORNYL ACETATE	11	1.1	1.8	1.9	1.4	(1)70.	(1)0.30	*Syrups* (1)0.20
2160 *iso*-BORNYL ACETATE	8	9.6	12.	3.9	9.5	(1)70.		

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FEMA No. and Substance	No. of Reports	Beverages	Ice Cream, Ices, Etc.	Candy	Baked Goods	Gelatins and Puddings	Chewing Gum	— Other Category Uses —	
2161 BORNYL FORMATE	5	3.7	0.30 3.0	0.80 2.0	0.80 2.0			*Syrups* (1)0.04	
2162 *iso*-BORNYL FORMATE	3	0.06 1.0	0.03 1.0	0.74	(1)0.80				
2163 *iso*-BORNYL PROPIONATE	3	0.01 1.0	0.80 1.0	1.2	(1)1.8				
2164 BORNYL VALERATE	3	0.06 1.0	(1)0.30	0.90 2.0	(1)0.80				
2165 BORNYL *iso*-VALERATE Bornyval	3	0.06 1.0	0.40 1.0	0.90 2.0	0.90 2.0			*Syrups* (1)1.2	
2166 *iso*-BORNYL *iso*-VALERATE	3	0.60 1.0	0.30 1.0	0.90	0.80 2.0				
2167 BORONIA, ABSOLUTE--*Boronia megastigma* Nees	9	4.3	2.8	11.	10.				
2168 BROMINATED VEGETABLE OILS	62	170.	260.	-	35. 190.				
2169 BUCHU LEAVES, OIL--*Barosma betulina* Bartl. et Wendl., *B. crenulata* (L.) Hook., or *B. serratifolia* Willd.	12	1.9	6.8	8.5	5.2			*Alcoholic Beverages* (1)0.50	*Condiments* (1)7.0
2170 2-BUTANONE--Methyl ethyl ketone; MEK	1	(1)70.	(1)270.	(1)100.	(1)100.				
2171 BUTTER ACIDS[b]	5	(1)2.0	(1)3.0	2,800.	8.3				
2172 BUTTER ESTERS[c]	13	-	24.	78.	86.			Popcorn Oil (1)1,200.	Toppings (1)2.0
2173 BUTTER STARTER DISTILLATE	10	-	20. 40.	420.	720.			*Shortening* 750. 12,000.	
2174 BUTYL ACETATE	24	11.	16.	32.	32.	13.	220.		
2175 *iso*-BUTYL ACETATE	28	11.	16.	36.	35.	170.	860.	*Icings* (1)6.5	
2176 BUTYL ACETOACETATE	3	4.2	7.3	26.	26.				
2177 *iso*-BUTYL ACETOACETATE	3	4.0	7.0	25.	25.				
2178 BUTYL ALCOHOL--1-Butanol	9	12.	7.0	34.	32.			*Alcoholic Beverages* (1)1.0	*Cream* (1)4.0
2179 *iso*-BUTYL ALCOHOL--*iso*-Butanol	6	17.	7.0	30.	24.				
2180 *iso*-BUTYL ANGELATE--*iso*-Butyl *cis*-2-methyl-2-butenoate	2	(1)1.5	(1)1.5	(1)5.0	-			*Icings* 3.0 100.	
2181 BUTYL ANTHRANILATE	10	1.3	2.6	9.0	6.7				
2182 *iso*-BUTYL ANTHRANILATE	10	2.0	4.0	12.	12.		5.0 1,700.		
2183 BUTYLATED HYDROXYANISOLE--Mixture of 2-*tert*-Butyl-4-methoxyphenol and 3-*tert*-Butyl-4-methoxyphenol; BHA; Embanox	34	0.82	0.81	9.6	2.8	0.54	13.	*Potatoes* (1)5.0	*Shortening* 230.
2184 BUTYLATED HYDROXYTOLUENE--2,6-di-*tert*-Butyl *p*-cresol; BHT; 2,6-di-*tert*-Butyl-4-methylphenol; Ionol C.P.; Impruvol; Vianol; Parabar	0	-	-	-	-	-			
2185 *iso*-BUTYL BENZOATE	5	2.0 9.0	7.9	12.	10. 23.				
2186 BUTYL BUTYRATE	21	8.6	22.	24.	22.	14.	150. 1,500.		
2187 *iso*-BUTYL BUTYRATE	16	8.3	16.	25.	24.	14.	(1)2,000.	*Alcoholic Beverages* (1)2.0	
2188 BUTYL *iso*-BUTYRATE	12	8.7	4.0 5.0	19.	39.		(1)2,000.		

[b] Assuming that these are a mixture consisting only of the saponified acids reported in the literature as derived from butter in the approximate proportions normally occurring.

[c] Assuming that these are the ethyl esters of butter acids (q.v.).

FEMA No. and Substance	No. of Reports	Beverages	Ice Cream, Ices, Etc.	Candy	Baked Goods	Gelatins and Puddings	Chewing Gum	— Other Category Uses —		
2189 -BUTYL *iso*-BUTYRATE	10	7.5	7.4	16.	17.	3.3 10.		*Alcoholic Beverages* (1)2.0		
190 BUTYL BUTYRYLLACTATE--Lactic acid, butyl ester, butyrate	15	13.	9.0	44.	58.					
2191 α-BUTYLCINNAMALDEHYDE	4	0.50 1.0	1.0 2.8	2.0 8.0	2.0 8.0					
2192 BUTYL CINNAMATE	5	0.83	2.6	1.0 15.	1.0 15.			*Alcoholic Beverages* (1)2.0		
2193 *iso*-BUTYL CINNAMATE	7	3.3	3.4	5.4	5.4			*Alcoholic Beverages* (1)2.0		
2194 BUTYL 2-DECENOATE--Butyl decylenate	2	(1)8.0	-	1.5 22.	(1)30.		(1)2,000.			
2195 BUTYL ETHYL MALONATE	2	(1)3.0	-	(1)0.13	-					
2196 BUTYL FORMATE	8	2.9	3.2	11.	9.1	(1)5.0				
2197 *iso*-BUTYL FORMATE--Tetryl formate	10	2.2	7.1	19.	8.2	(1)5.0				
2198 *iso*-BUTYL 2-FURANPROPIONATE--*iso*-Butyl furylpropionate	7	8.1	14.	17.	21.	4.0 30.	(1)12.	*Icings* (1)20.		
2199 BUTYL HEPTANOATE	2	0.50 1.0	2.0 10.	2.0 25.	2.0 25.					
2200 *iso*-BUTYL HEPTANOATE	2	0.50 1.5	2.4 10.	7.0 25.	7.0 25.					
2201 BUTYL HEXANOATE	6	1.7	3.9	7.6	10.					
2202 *iso*-BUTYL HEXANOATE	8	5.4	3.9	8.1	8.3		(1)2.0			
2203 TYL *p*-HYDROXYBENZOATE--Butyl parasept	2	(1)1,000.	-	-	(1)10.					
2204 2-BUTYL-5 or 6-KETO-1,4-DIOXANE	1	-	(1)5.0	(1)5.0	(1)5.0			*Shortening* (1)5.0		
2205 BUTYL LACTATE	3	0.66	2.8	6.5	7.7					
2206 BUTYL LAURATE--Butyl dodecanoate	4	0.40 3.0	(1)0.60	17.	1.0 40.					
2207 BUTYL LEVULINATE	3	0.20 1.0	3.1	4.6	4.6					
2208 α-*iso*-BUTYLPHENETHYL ALCOHOL--4-Methyl-1-phenyl-2-pentanol; Benzyl *iso*-butyl carbinol; Benzyl *iso*-amyl alcohol	3	1.0 10.	38.	54.	18. 60.			*Alcoholic Beverages* (1)50.		
2209 BUTYL PHENYLACETATE	7	0.50	2.1	4.5	4.6	(1)5.0				
2210 *iso*-BUTYL PHENYLACETATE	11	2.8	2.8	5.5	8.0	(1)5.0		*Maraschino Cherries* (1)3.0		
2211 BUTYL PROPIONATE	10	4.0	5.2	28.	27.					
2212 *iso*-BUTYL PROPIONATE	10	5.4	4.2	23.	35.					
2213 *iso*-BUTYL SALICYLATE	7	3.5	1.8	2.6	5.0					
2214 BUTYL STEARATE--Butyl octadecanoate	5	(1)1.0	(1)2.0	190.	340.		(1)330.	*Alcoholic Beverages* (1)5.0		
2215 BUTYL SULFIDE--Dibutyl sulfide	2	0.02 1.0	0.01 1.0	0.03 1.0	0.03 1.0					
2216 BUTYL 10-UNDECENOATE	5	0.90	2.0	6.6	7.8		0.40 60.	*Alcoholic Beverages* (1)5.0	*Icings* (1)5.0	
2217 BUTYL VALERATE	5	3.0	2.6	8.0	6.8					
2218 BUTYL *iso*-VALERATE	7	4.6	12.	13.	18.	(1)50.				

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FEMA No. and Substance	No. of Reports	Beverages	Ice Cream, Ices, Etc.	Candy	Baked Goods	Gelatins and Puddings	Chewing Gum	— Other Category Uses —		
2219 BUTYRALDEHYDE--Butanal; Butyl aldehyde; Butyric aldehyde	6	0.71	4.8	2.9	5.4			*Alcoholic Beverages* (1)0.50	*Icings* (1)0.25	
2220 *iso*-BUTYRALDEHYDE--2-Methyl propanal; *iso*-Butyl aldehyde, *iso*-Butyric aldehyde	4	0.30	0.25 0.50	0.67	0.50 1.0			*Alcoholic Beverages* (1)5.0		
2221 BUTYRIC ACID--Ethylacetic acid; Butanoic acid	54	5.5	6.5	82.	32.	0.19 45.	60. 270.	*Margarine* 18.		
2222 *iso*-BUTYRIC ACID--2-Methyl propanoic acid; *iso*-Propylformic acid	16	4.1	12.	41.	38.		(1)470.	*Margarine* (1)30.		
2223 (tri-)BUTYRIN--Glyceryl tributyrate; Butyrin	5	(1)0.10	(1)0.04	0.33 1,000.	290.	(1)0.36		*Margarine* 2.0 50.		
2224 CAFFEINE--1,3,7-Trimethylxanthine; 1,3,7-Trimethyl-2,6-dioxopurine; Coffeine; Theine; Guaranine; Methyltheobromine; No-Doz®	24	120.	-	-	-					
2225 CAJEPUT OIL--*Melaleuca leucadendron* L.	5	0.50 2.0	(1)1.0	13.	11.					
2226 CALAMUS [*Acorus calamus* L.]--Sweet Flag	6	68.	(1)1.0	(1)10.	(1)15.			*Alcoholic Beverages* (1)30.	*Bitters* (1)3,000.	
2227 CALAMUS OIL [*Acorus calamus* L.]--Sweet flag, oil	16	2.0	1.5	3.0	3.8	(1)0.02		*Alcoholic Beverages* 5.0 15.		
2228 CALCIUM ACETATE--Sorbo-Calcion, technical product known as Brown or Gray Acetate of Lime	2	(1)200.	-	-	(1)500.					
2229 CAMPHENE--2,2-Dimethyl-3-methylenenorbornane	4	40. 90.	(1)20.	(1)160.	27.					
2230 *d*-CAMPHOR	4	-	(1)0.10	1.1 25.	11.			*Condiments* (1)20.		
2231 CAMPHOR, JAPANESE, WHITE, OIL--*Cinnamomum camphora* (L.) Nees et Eberm.	5	5.4	-	-	1.6 48.			*Condiments* (1)15.		
2232 *CANANGA OIL--*Cananga odorata* Hook. f. and Thoms.	4	7.0	(1)1.0	(1)2.0	(1)2.0					
2233 *CAPSICUM, EXTRACT--*Capsicum frutescens* L.; C. *annuum* L.	8	120.	(1)15.	(1)12.	12. 14.			*Condiments* 50. 100.	*Meats* (1)200.	
2234 *CAPSICUM, OLEORESIN--*Capsicum frutescens* L.; C. *annuum* L.	49	14.	-	11.	(1)14.		46.	*Condiments* 93.	*Meats* 50. 100.	
2235 CARAMEL COLOR	123	2,200.	590.	180.	220.			*Meats* 3,100.	*Syrups* 2,800.	
2236 *CARAWAY--*Carum carvi* L.	7	(1)63.	(1)63.	-	3,000. 10,000.			*Condiments* (1)96.		
2237 *CARAWAY, BLACK--*Nigella sativa* L.	0	-	-	-	-					
2238 *CARAWAY, OIL--*Carum carvi* L.	33	29.	49.	86.	150.		(1)0.80	*Alcoholic Beverages* 140.	*Condiments* 38.	*Meats* 34.
2239 CARBOXYMETHYLCELLULOSE	23	91.	670.	9.0	41.			*Condiments* (1)2,000.	*Icings & Toppings* 2,300.	*Meats* (1)100.
2240 *CARDAMOM--*Elletaria cardamomum* (L.) Maton	22	3.0	(1)2.0	(1)2.0	1,700.			*Condiments* (1)900.	*Meats* 570.	
2241 *CARDAMOM SEED, OIL--*Elletaria cardamomum* (L.) Maton	37	1.9	1.3	5.8	57.		(1)2.2	*Alcoholic Beverages* 10. 10.	*Pickles* 10. 16.	*Condiments* 8.0 *Meats* 36.
2242 CARMINE--*Coccus cacti* L.	5	-	-	10. 100.	7.0 300.			*Condiments* (1)200.	*Meats* (1)40.	
2243 *CAROB BEAN, EXTRACT [*Ceratonia siliqua* L.]--St. John's bread	33	66.	93.	180.	120.	600.		*Icings & Toppings* 500. 1,000.		
2244 *CARROT OIL--*Daucus carota* L.	13	3.1	5.5	5.1	4.4	(1)0.02		*Condiments* (1)15.	*Soups* (1)1.0	

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FEMA No. and Substance	No. of Reports	Beverages	Ice Cream, Ices, Etc.	Candy	Baked Goods	Gelatins and Puddings	Chewing Gum	— Other Category Uses —		
2245 RVACROL--2-p-Cymenol; 2-Methyl-5-*iso*-propylphenol; *iso*-Thymol; Cymophenol; 2-Hydroxy-p-cymene; *iso*-Propyl o-cresol	9	26.	34.	92.	120.			*Condiments* 37.		
2246 CARVACRYL ETHYL ETHER--2-Ethoxy-p-cymene; Ethyl carvacrol	3	2.0 13.	(1)10.	21.	3.0 39.					
2247 CARVEOL--p-Mentha-6,8-dien-2-ol	3	1.5 13.	(1)3.0	3.0 39.	3.0 5.0					
2248 4-CARVOMENTHENOL--1-p-Menthen-4-ol; 4-Terpinenol; 1-Methyl-4-*iso*-propyl-1-cyclohexene-4-ol; Origanol	3	1.0 21.	1.0 84.	7.0 63.	(1)7.0					
2249 CARVONE--6,8(9)-p-Menthadien-2-one; Carvol	20	850.	120.	180.	110.			*Alcoholic Beverages* 130.		
2250 CARVYL ACETATE	3	1.5 11.	3.0 44.	20.	20.					
2251 CARVYL PROPIONATE	2	(1)1.0	(1)2.0	2.0 24.	2.0 24.					
2252 β-CARYOPHYLLENE	9	14.	(1)2.0	34.	27.		(1)200.	*Condiments* (1)50.		
2253 CASCARA, BITTERLESS, EXTRACT--*Rhamnus purshiana* DC.	4	(1)100.	(1)50.	-	(1)100.					
2254 *CASCARILLA BARK, EXTRACT--*Croton cascarilla* Benn. and *C. eluteria* Benn.	2	5.0 800.	-	-	-					
2255 *CASCARILLA BARK, OIL--*Croton cascarilla* Benn. and *C. eluteria* Benn.	9	2.3	3.0	8.7	13.			*Condiments* (1)80.		
2256 *CASSIA--*Cinnamomum cassia* Blume	33	9.2	5.1	130.	3,000.					
2257 ASSIA BARK, EXTRACT--*Cinnamomum cassia* Blume	5	310.	(1)10.	(1)10.	(1)10.					
2258 *CASSIA BARK, OIL--*Cinnamomum cassia* Blume--	66	3.0	11.	150.	73.		1,900.	*Condiments* 140.	*Meats* 290.	
2259 *CASSIA BUDS [*Cinnamomum cassia* Blume] Cinnamon flowers; Cassia flowers	1	(1)1,000.	-	-	-					
2260 CASSIE, ABSOLUTE--*Acacia farnesiana* (L.) Willd.	7	0.96	1.2	4.1	4.1	(1)1.0				
2261 *CASTOREUM, EXTRACT--*Castor fiber* L. and *C. canadensis* Kuhl	19	5.0	5.6	12.	41.		(1)400.	*Condiments* (1)50.	*Toppings* (1)2.0	
2262 *CASTOREUM, LIQUID--*Castor fiber* L. and *C. canadensis* Kuhl	23	3.2	1.9	4.9	7.3	1.2 2.0	19. 60.	*Toppings* (1)2.0		
2263 CASTOR, OIL [*Ricinus communis* L.]--Ricinus, oil; Palma Christi, oil; Tangantangan, oil	11	1.5 140.	3.0 540.	3.0 410.	210.					
2264 CATECHU, EXTRACT [*Acacia catechu* Willd.]--Black cutch, extract; Cachou, extract; Pegu catechu, extract; Cashoo, extract	7	16.	21.	140.	140.					
2265 CATECHU, POWDER [*Acacia catechu* Willd.]--Gambir, gum; Pale catechu; Gambir catechu; Terra Japonica	10	45.	27.	43.	37.		(1)15.			
2266 *CAYENNE--*Capsicum annuum* L. var. *longum* Sendt	22	(1)1.0	(1)2.0	(1)2.0	2.0 50.			*Condiments* 610.	*Meats* 910.	*Soups* (1)100.
2267 CEDAR LEAF, OIL[4] --*Thuja occidentalis* L.	11	0.01 0.50	0.01 1.0	12.	1.0 20.			*Alcoholic Beverages* (1)16.	*Meats* (1)15.	
2268 CELERY SEED--*Apium graveolens* L.	29	0.37 1,000.	-	-	1,800.			*Condiments* 2,500.	*Meats* 1,400. *Soups* 37,500.	*Pickles* 13,590.

[4] Provided it is used at levels such that no thujone is detectable in the finished food, using the standard AOAC method.

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FEMA No. and Substance	No. of Reports	Beverages	Ice Cream, Ices, Etc.	Candy	Baked Goods	Gelatins and Puddings	Chewing Gum	—Other Category Uses—		
2269 *CELERY SEED, EXTRACT--*Apium graveolens* L.	15	240.	(1)5.0	(1)10.	1,900.			Condiments (1)10.	Meats (1)100.	Soups 160. 500.
2270 *CELERY SEED, EXTRACT SOLID--*Apium graveolens* L.	5	(1)150.	-	(1)8.0	(1)12.			Condiments (1)7.0	Syrups (1)10.	
2271 *CELERY SEED, OIL--*Apium graveolens* L.	42	11.	3.0 13.	13.	12.		(1)28.	Condiments 40.	Meats 40. Pickles 10. 35.	Soups (1)1.0
2272 *CHAMOMILE FLOWER, ENGLISH, OIL--*Anthemis nobilis* L.	4	4.1	0.10 0.50	1.3 5.0	0.10 5.0					
2273 *CHAMOMILE FLOWER, HUNGARIAN, OIL--*Matricaria chamomilla* L.	8	2.6	6.1	3.8	6.5		(1)0.80	Alcoholic Beverages (1)1.0		
2274 *CHAMOMILE FLOWER, ROMAN, EXTRACT--*Anthemis nobilis* L.	8	13.	9.3	6.7	16.					
2275 *CHAMOMILE FLOWER, ROMAN, OIL--*Anthemis nobilis* L.	10	2.3	3.3	4.3	4.3	(1)0.25		Alcoholic Beverages (1)20.		
2276 *CHERRY BARK, WILD, EXTRACT--*Prunus serotina* Ehrh.	35	120.	140.	200.	76.	(1)3.5		Alcoholic Beverages 300. 800.	Syrups (1)30.	
2277 CHERRY LAUREL, OIL (FFPA)--*Prunus laurocerasus* L.	5				(1)75.			Maraschino Cherries (1)77.	Extracts 50. 65.	
2278 CHERRY PITS, EXTRACT--*Prunus avium* L. (sweet cherry); *P. cerasus* L. (sour cherry)	6	80. 150.	50. 60.	-	-					
2279 *CHERVIL--*Anthriscus cerefolium* (L.) Hoffm.	4	(1)100.	(1)80.	-	(1)150.			Condiments (1)60.		
2280 *CHICORY, EXTRACT--*Cichorium intybus* L.	19	63.	58.	57.	100.					
2281 CINCHONA BARK, RED--*Cinchona succirubra* Pav. or its hybrids	9	1.5 3.7	(1)3.0	(1)3.0	27.			Alcoholic Beverages 20. 300.	Bitters (1)1,000.	
2282 CINCHONA BARK, RED, EXTRACT--*Cinchona succirubra* Pav. or its hybrids	3	(1)100.	(1)25.	-	(1)20.			Condiments (1)60.		
2283 *CINCHONA BARK, YELLOW--*Cinchona ledgeriana* Moens, *C. calisaya* Wedd., or hybrids of these with other spp. of *Cinchona*	4	-	-	-	-			Alcoholic Beverages (1)300.	Bitters (1)100.	
2284 CINCHONA BARK, YELLOW, EXTRACT--*Cinchona ledgeriana* Moens. *C. calisaya* Wedd., or hybrids of these with other spp. of *Cinchona*	4	(1)100.*	-	-	-					
2285 CINCHONA, EXTRACT [*Cinchona ledgeriana* Moens et Trimen. *C. succirubra* Pavon et Klotzsch or its hybrids; *C. calisaya* Wedd., or hybrids of these with other *Cinchona* spp.]--Quinine, extract	4	(1)10.	-	(1)1.0	-					
2286 CINNAMALDEHYDE--Cinnamic aldehyde; 3-Phenylpropenal; Phenylacrolein; Cinnamal	51	9.0	7.7	700.	180.		4,900.	Condiments (1)20.	Meats (1)60.	
2287 CINNAMALDEHYDE ETHYLENE GLYCOL ACETAL--Cinnclovel	2	-	-	0.06 2.0	(1)2.0			Condiments (1)5.0		
2288 CINNAMIC ACID--β-Phenylacrylic acid; 3-Phenylpropenoic acid	10	31.	40.	30.	36.		(1)10.			
2289 *CINNAMON [*Cinnamomum zeylanicum* Nees; *C. loureirii* Blume, *C. cassia* Blume]--Ceylon cinnamon; Chinese cinnamon; Saigon cinnamon	43	5.6	53.	10. 4,000.	1,900.			Apple Butter 78. 450.	Condiments (1)110.	Meats 880.
2290 *CINNAMON BARK, EXTRACT--*Cinnamomum zeylanicum* Nees, *C. loureirii* Blume; *C. cassia* Blume	6	10. 13.	(1)8.5	-	(1)170.			Condiments 40. 200.	Meats (1)40.	

* Probably alcoholic beverages

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2291 *CINNAMON BARK, OIL--*Cinnamomum zeylanicum* Nees; *C. loureirii* Blume, *C. cassia* Blume	33	5.5	18.	80.	110.		620.	*Condiments* (1)25.	*Meats* (1)50.	
2292 *CINNAMON LEAF, OIL [*Cinnamomum zeylanicum* Nees; *C. loureirii* Blume; *C. cassia* Blume]--Ceylon cinnamon leaf, oil; Chinese cinnamon leaf, oil; Saigon cinnamon leaf, oil	24	6.8	3.4	32.	54.	(1)0.20	160. 520.	*Condiments* 20. 78.	*Pickles* 32. 48.	*Spiced Fruits* (1)3.0
2293 CINNAMYL ACETATE	32	2.7	6.5	16.	11.		(1)8.7	*Condiments* 2.0 2.0		
2294 CINNAMYL ALCOHOL--3-Phenyl-2-propen-1-ol; Cinnamic alcohol; Styryl carbinol; γ-Phenylallyl alcohol	19	8.8	8.7	17.	33.	(1)22.	720.	*Alcoholic Beverages* (1)5.0		
2295 CINNAMYL ANTHRANILATE	14	6.8	1.7	4.3	5.3	(1)28.	46. 730.			
2296 CINNAMYL BUTYRATE	11	1.6	8.5	7.6	11.	(1)1.2				
2297 CINNAMYL *iso*-BUTYRATE	16	1.5	5.0	7.7	8.5	0.02 1.2	(1)140.	*Toppings* (1)1.0		
2298 CINNAMYL CINNAMATE--Phenylallyl cinnamate; Styracin	4	0.81	1.5	10.	7.0					
2299 CINNAMYL FORMATE	10	1.3	9.1	6.9	8.0		(1)0.60			
2300 CINNAMYL PHENYLACETATE	5	2.7	0.25 2.0	7.3	7.3					
2301 CINNAMYL PROPIONATE--γ-Phenylallyl propionate; 3-Phenyl-2-propenyl propanoate	22	1.0	4.3	7.5	8.8	2.4 4.0	20. 53.			
2302 CINNAMYL *iso*-VALERATE	21	2.2	2.6	4.1	3.6	11.	19. 30.			
2303 CITRAL--3,7-Dimethyl-2,6-octadienal; Geranial	78	9.2	23.	41.	43.		170.			
2304 CITRAL DIETHYL ACETAL--3,7-Dimethyl-2,6-octadienal diethyl acetal	3	(1)0.03	-	(1)0.13	-			*Condiments* (1)110.		
2305 CITRAL DIMETHYL ACETAL--3,7-Dimethyl-2,6-octadienal dimethyl acetal	3	6.3	11.	60.	60.		(1)15.			
2306 CITRIC ACID--2-Hydroxy-1,2,3-propanetricarboxylic acid; β-Hydroxytricarballylic acid	89	2,500.	1,600.	4,300.	1,200.		3,600.			
2307 CITRONELLAL--3,7-Dimethyl-6-octenal; Rhodinal	16	4.0	1.3	4.5	4.7	(1)0.60	(1)0.30			
2308 *CITRONELLA, OIL--*Cymbopogon nardus* Rendle	6	17.	26.	25.	31.					
2309 *dl*-CITRONELLOL--3,7-Dimethyl-6-octen-1-ol (commercial Citronellol is largely *dl*-)	16	4.1	4.1	16.	18.	5.8	29. 52.			
2310 CITRONELLOXYACETALDEHYDE--6,10-Dimethyl-3-oxa-9-undecenal	3	0.005 1.0	1.4	4.1	4.3					
2311 CITRONELLYL ACETATE--3,7-Dimethyl-6-octen-1-yl acetate	13	3.4	4.2	7.5	9.7	0.71 3.7	6.9 600.			
2312 CITRONELLYL BUTYRATE--3,7-Dimethyl-6-octen-1-yl butyrate	13	3.8	11.	13.	11.	3.1 4.2	(1)2.3			
2313 CITRONELLYL *iso*-BUTYRATE--3,7-Dimethyl-6-octen-1-yl *iso*-butyrate	8	2.3	1.7	8.2	12.	(1)3.1				
2314 CITRONELLYL FORMATE--3,7-Dimethyl-6-octen-1-yl formate	7	14.	13.	19.	32.		63. 100.			
2315 CITRONELLYL PHENYLACETATE--3,7-Dimethyl-6-octen-1-yl phenylacetate	6	1.3	0.95	2.4	17.					

FEMA No. and Substance	No. of Reports	Beverages	Ice Cream, Ices, Etc.	Candy	Baked Goods	Gelatins and Puddings	Chewing Gum	— Other Category Uses —		
2316 .ITRONELLYL PROPIONATE–3,7-Dimethyl-6-octen-1-yl propionate	7	3.1	9.0	18.	19.		0.80 15.			
2317 CITRONELLYL VALERATE–3,7-Dimethyl-6-octen-1-yl valerate	4	1.0	2.5	3.0	7.7					
2318 *CITRUS PEELS, EXTRACT–*Citrus* spp.	10	190.	420.	480.	480.					
2319 *CIVET, ABSOLUTE–Civet cats: *Viverra civetta* Schreber and *V. zibetha* Schreber	10	1.0	3.0	3.7	2.8	(1)0.10	(1)2.2			
2320 *CLARY [*Salvia sclarea* L.]–Clary sage	2	-	-	-	-			*Alcoholic Beverages* (1)500.		
2321 *CLARY, OIL [*Salvia sclarea* L.]–Clary sage, oil	18	1.8	3.9	5.3	13.			*Alcoholic Beverages* (1)100.	*Condiments* (1)20.	
2322 *CLOVE BUD, EXTRACT–*Eugenia caryophyllata* Thunb. [*Eugenia aromatica* (L.) Baill.]	7	16.	19.	2.0 20.	48.			*Condiments* (1)150.	*Meats* 160. 250.	
2323 *CLOVE BUD, OIL–*Eugenia caryophyllata* Thunb. [*Eugenia aromatica* (L.) Baill.]	76	3.1	13.	320.	37.	0.33 5.0	1,800.	*Alcoholic Beverages* (1)300. *Meats* 75.	*Condiments* 55. *Spiced Fruits* 830.	*Jellies* (1)7.3
2324 *CLOVE BUD, OLEORESIN–*Eugenia caryophyllata* Thunb. [*Eugenia aromatica* (L.) Baill.]	5	-	-	-	-			*Meats* 100.		
2325 *CLOVE LEAF, OIL–*Eugenia caryophyllata* Thunb. [*Eugenia aromatica* (L.) Baill.]	21	8.6	16.	22.	30.	(1)5.0		*Apple Butter* (1)2.0 *Pickles* 7.0 16.	*Condiments* 14. 40.	*Meats* 670.
2326 *CLOVER TOPS, RED, EXTRACT SOLID [*Trifolium pratense* L.]–Trifolium, extract solid	2	(1)2.0	(1)3.0	(1)20.	(1)9.0					
2327 *CLOVES–*Eugenia caryophyllata* Thunb. [*Eugenia aromatica* (L.) Baill.]	32	20. 1,000.	33.	-	1,200.			*Spiced Cherries* (1)500.	*Meats* 810.	
2328 *CLOVE STEM, OIL–*Eugenia caryophyllata* Thunb. [*Eugenia aromatica* (L.) Baill.]	11	5.9	4.0 7.0	91.	64.			*Condiments* 30. 70.		
2329 *COCA LEAF, EXTRACT (DECOCAINIZED)–*Erythroxylon coca* Lam.	7	200.	(1)540.	(1)400.	-					
2330 COCHINEAL–*Coccus cacti* L.	5	(1)100.	-	36.	(1)300.			*Condiments* (1)200.		
2331 *COGNAC, GREEN, OIL	44	5.2	8.2	12.	14.		56.	*Alcoholic Beverages* 390.	*Condiments* (1)1.0	
2332 *COGNAC, WHITE, OIL	19	5.6	14.	18.	24.	(1)0.10				
2333 *CORIANDER–*Coriandrum sativum* L.	20	7.4	(1)1.0	1.0 20.	800.			*Alcoholic Beverages* (1)1,000.	*Condiments* (1)54.	*Meats* 1,300.
2334 *CORIANDER, OIL–*Coriandrum sativum* L.	60	3.1	4.5	8.8	9.3		7.4	*Alcoholic Beverages* 10. 30.	*Condiments* 12.	*Meats* 47.
2335 *CORN SILK–*Zea mays* L.	4	16. 28.	5.5 10.	12. 18.	12. 21.					
2336 COSTUS ROOT, OIL [*Saussurea lappa* Clarke (*Aplotaxis lappa* Dec., *A. auriculata* DC., *Aucklandia costus* Falc.)]–Spiral flag, oil	7	0.08	0.90	1.9	1.2	(1)0.10				
2337 p-CRESOL–4-Cresol	3	0.67	0.01 1.0	0.01 2.0	0.01 2.0					
2338 CUBEBS–*Piper cubeba* L. f.	4	(1)800.	-	-	-					
2339 CUBEBS, OIL–*Piper cubeba* L. f.	13	2.4	(1)0.25	1.8	4.6			*Condiments* 33.	*Meats* 25. 30.	

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2340 *CUMIN--*Cuminum cyminum* L.	18	.	.	.	(1)2,500.			*Condiments* 300. 3,900.	*Meats* 1,000.	
2341 CUMINALDEHYDE--*p-iso*-Propyl benzaldehyde; Cuminal; Cuminic aldehyde; Cumaldehyde	16	3.1	3.2	4.0	4.0		0.40 0.50	*Condiments* (1)3.0		
2342 *CUMIN, BLACK--*Nigella sativa* L.	0	.	.	.	.					
2343 *CUMIN, OIL--*Cuminum cyminum* L.	20	0.48	0.66	7.3	10.		(1)0.20	*Condiments* 230.	*Meats* 40. 100.	*Pickles* (1)40.
2344 *CURACAO PEEL, EXTRACT--*Citrus aurantium* L.	3	1,700.	.	.	.					
2345 *CURACAO PEEL, OIL--*Citrus aurantium* L.	5	33.	0.80 20.	43.	4.0 100.					
2346 CURRANT BUDS, BLACK, ABSOLUTE [*Ribes nigrum* L.]--Cassis	4	4.7	(1)8.0	(1)20.	(1)20.	(1)5.0				
2347 CYCLOHEXANEACETIC ACID--Cyclohexylacetic acid	2	(1)1.0	(1)2.0	(1)2.0	(1)2.0					
2348 CYCLOHEXANEËTHYL ACETATE--Cyclohexylethyl acetate	1	(1)2.0	(1)3.0	(1)6.0	(1)20.					
2349 CYCLOHEXYL ACETATE	10	20.	15.	100.	110.					
2350 CYCLOHEXYL ANTHRANILATE	3	10.	3.7	3.7	2.0 10.	(1)1.0				
2351 CYCLOHEXYL BUTYRATE	14	3.9	5.7	9.2	28.	(1)0.54				
2352 CYCLOHEXYL CINNAMATE	4	2.0	1.0 5.0	4.0 10.	4.0 20.					
2353 CYCLOHEXYL FORMATE	4	11.	2.8	8.0	7.0 10.					
2354 CYCLOHEXYL PROPIONATE	3	2.4	2.7	2.0 3.0	(1)3.0	(1)5.0				
2355 CYCLOHEXYL *iso*-VALERATE	7	13.	7.0 25.	9.3	1.7 60.					
2356 *p*-CYMENE--Cymene; Cymol	9	3.3	5.3	10.	7.0		(1)250.	*Condiments* 10. 130.		
2357 *DANDELION, FLUID EXTRACT--*Taraxacum officinale* Weber; *T. erythrospermum* Andrz.	5	35.	6.0	2.0 8.0	53.					
2358 *DANDELION ROOT, EXTRACT SOLID--*Taraxacum officinale* Weber; *T. erythrospermum* Andrz.	5	10.	2.5 20.	8.0 40.	27.					
2359 DAVANA, OIL--*Artemisia pallens* Wall.	4	3.0	6.5	8.0	11.		(1)5.0			
2360 γ-DECALACTONE--4-Hydroxydecanoic acid, γ-lactone	10	2.0	4.5	5.7	7.1	0.08 8.0				
2361 δ-DECALACTONE--5-Hydroxydecanoic acid, δ-lactone	4	5.0 5.0	(1)10.	0.25 5.0	0.25 8.0			*Toppings* (1)5.0		
2362 DECANAL--Capraldehyde; Capric aldehyde; Caprinaldehyde; Aldehyde C-10	24	2.3	4.1	5.7	6.6	(1)3.0	0.60			
2363 DECANAL DIMETHYL ACETAL--1,1-Dimethoxydecane	3	1.0 2.0	(1)2.0	(1)8.0	(1)8.0	(1)3.0		*Alcoholic Beverages* (1)8.0		
2364 DECANOIC ACID--Capric acid; Decylic acid	14	9.9	3.1	4.5	7.8	0.10 3.0		*Shortening* (1)6.0		
2365 1-DECANOL--Decyl alcohol; Decylic alcohol; Nonylcarbinol; Alcohol C-10	16	2.1	4.6	5.2	5.2		(1)3.0			
2366 2-DECENAL--Decenaldehyde	5	3.4	6.0	9.0	9.0					
2367 DECYL ACETATE--Decanyl acetate; Acetate C-10	12	3.4	2.7	6.1	10.	(1)1.2	(1)12.			
2368 DECYL BUTYRATE	4	0.18	1.4	5.9	7.5					

FEMA No. and Substance	No. of Reports	Beverages	Ice Cream, Ices, Etc.	Candy	Baked Goods	Gelatins and Puddings	Chewing Gum	— Other Category Uses —		
2369 DECYL PROPIONATE	4	0.81	1.4	5.9	7.5					
2370 DIACETYL--2,3-Butanedione, Biacetyl; Dimethyl ketone; Dimethylglyoxal, 2,3-Diketobutane	63	2.5	5.9	21.	44.	19.	35.	*Shortening* 11.		
2371 DIBENZYL ETHER	6	8.3	5.6	23.	25.		85. 160.			
2372 4,4-DIBUTYL-γ-BUTYROLACTONE--4,4-Dibutyl-4-hydroxybutyric acid, γ-lactone	2	-	2.8 3.5	4.4 15.	(1)15.					
2373 DIBUTYL SEBACATE--Butyl sebacate	2	1.0 5.0	2.0 5.0	(1)15.	(1)15.					
2374 DIETHYL MALATE--Ethyl malate	3	5.5	6.5	18.	44.	(1)1.5				
2375 DIETHYL MALONATE--Ethyl malonate, Malonic ester	15	5.6	17.	20.	19.	(1)20.				
2376 DIETHYL SEBACATE--Ethyl sebacate	22	4.1	9.1	21.	41.	3.2 19.	2.7 450.			
2377 DIETHYL SUCCINATE	11	7.3	11.	38.	45.					
2378 DIETHYL TARTRATE	1	(1)50.	(1)200.	(1)200.	(1)200.					
2379 DIHYDROCARVEOL--8-p-Menthen-2-ol; 6-Methyl-3-*iso*-propenylcyclohexanol	3	(1)84.	(1)300.	10. 250.	10. 250.			*Alcoholic Beverages* (1)500.		
2380 DIHYDROCARVYL ACETATE--8-p-Menthen-2-yl acetate; 6-Methyl-3-*iso*-propenylcyclohexyl acetate	4	2.0 5.0	(1)20.	22.	22.			*Condiments* (1)10.		
2381 DIHYDROCOUMARIN--Hydrocoumarin; 1,2-Benzodihydropyrone	26	7.8	21.	44.	28.	10.	78.			
2382 *DILL--*Anethum graveolens* L.	14	-	-	-	(1)4,800.			*Condiments* 1,400.	*Meats* 1,200.	*Pickles* 8,200.
2383 *DILL, OIL--*Anethum graveolens* L.	31	1.6	5.8	9.9	5.0	(1)20.	3.8 8.0	*Alcoholic Beverages* (1)6.0 *Pickles* 140.	*Condiments* 150.	*Meats* 51.
2384 DILL SEED, INDIAN--*Anethum sowa* Roxb. (*Peucedanum graveolens* Benth. et Hook.; *A. graveolens* L.)	9	-	-	-	(1)400.			*Condiments* (1)200.	*Meats* 3.3 100.	
2385 *m*-DIMETHOXYBENZENE--Resorcinol dimethyl ether; 1,3-Dimethoxybenzene; Dimethyl resorcinol	6	3.0	5.0	5.0	8.0					
2386 *p*-DIMETHOXYBENZENE--Hydroquinone dimethyl ether; Dimethyl hydroquinone	14	8.1	5.0	4.7	5.8					
2387 2,4-DIMETHYLACETOPHENONE	6	0.78	0.77	3.9	2.7			*Alcoholic Beverages* (1)1.0		
2388 α,α-DIMETHYLBENZYL *iso*-BUTYRATE--Phenyl dimethyl carbinyl *iso*-butyrate	3	(1)5.0	(1)40.	(1)30.	(1)20.					
2389 2,6-DIMETHYL-5-HEPTENAL--Melonal	11	2.8	1.7	8.4	19.	0.02 10.	(1)0.80			
2390 2,6-DIMETHYL OCTANAL--*iso*-Decylaldehyde	3	0.44	3.2	1.9	1.9					
2391 3,7-DIMETHYL-1-OCTANOL--Tetrahydrogeraniol	5	4.3	2.0 44.	15.	19.					
2392 α,α-DIMETHYLPHENETHYL ACETATE--Benzyl dimethyl carbinyl acetate, Benzylpropyl acetate	5	2.8	8.0	22.	19.		(1)2.9			
2393 α,α-DIMETHYLPHENETHYL ALCOHOL--Dimethyl benzyl carbinol; Benzylpropyl alcohol	8	3.3	3.2	4.0	4.9	(1)0.01	(1)100.	*Jellies* (1)3.2		
2394 α,α-DIMETHYLPHENETHYL BUTYRATE--Benzyl dimethyl carbinyl butyrate	1	(1)10.	(1)20.	(1)20.	-	(1)20.				

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FEMA No. and Substance	No. of Reports	Beverages	Ice Cream, Ices, Etc.	Candy	Baked Goods	Gelatins and Puddings	Chewing Gum	—Other Category Uses—		
2395 α,α-DIMETHYLPHENETHYL FORMATE--Benzyl dimethyl carbinyl formate	1	(1)2.0	(1)10.	(1)10.	-					
2396 DIMETHYL SUCCINATE	3	1.0 100.	(1)5.0	(1)15.	(1)15.		(1)5.0			
2397 1,3-DIPHENYL-2-PROPANONE--Dibenzyl ketone	4	1.7	4.5	9.5	13.					
2398 DISODIUM PHOSPHATE	18	350.	350.	-	(1)2,300.			*Meats* 50. 250.	*Toppings* 2,500.	
2399 DITTANY OF CRETE [*Origanum dictamnus* L.]--Cretan dittany; Spanish hops	4	(1)25.	-	-	(1)8.8					
2400 γ-DODECALACTONE--4-Hydroxydodecanoic acid, γ-lactone; γ-Octyl-γ-butyrolactone	7	3.3	4.3	13.	11.	0.15		*Jellies* (1)0.01		
2401 δ-DODECALACTONE--5-Hydroxydodecanoic acid, δ-lactone	2	-	-	(1)0.06	(1)0.06			*Toppings* (1)10.		
2402 2-DODECENAL	5	2.9	3.1	2.8	2.8					
2403 *DOGGRASS, EXTRACT [*Agropyron repens* (L.) Beauv.]--Agropyrum; Quack grass; Quick grass; Couch grass; Triticum; Graminis	2	(1)2.0	(1)4.0	(1)6.0	(1)6.0					
2404 DRAGON'S BLOOD, EXTRACT [*Daemonorops* spp. or other botanical sources]--Draco rubin, extract	2	(1)300.	-	-	-					
2405 *DULSE--*Rhodymenia palmata* (L.) Grev.	1	-	-	-	-					
2406 *ELDER FLOWERS--*Sambucus canadensis* L. or *S. nigra* L.	5	340.	(1)1.0	(1)1.0	(1)1.0			*Alcoholic Beverages* (1)25.		
2407 ELEMI, GUM--*Canarium commune* L. or *C. luzonicum* (Miq.) A. Gray	4	(1)0.13	(1)0.25	(1)0.25	(1)0.25					
2408 ELEMI, OIL--*Canarium commune* L. or *C. luzonicum* (Miq.) A. Gray	5	0.71	0.25 5.0	0.25 15.	7.5			*Soups* (1)10.		
2409 ERIGERON, OIL [*Erigeron canadensis* L.]--Fleabane, oil	5	0.13 4.8	0.25 3.5	0.26 30.	0.25 1.0			*Condiments* (1)2.0		
2410 ERYTHORBIC ACID--Araboascorbic acid; *iso*-Ascorbic acid	15	100.	(1)20.	-	(1)500.	*		*Meats* 380.		
2411 ESTRAGOLE--*p*-Allylanisole; Methyl chavicol; Chavicyl methyl ether; Esdragol; *p*-Methoxyallylbenzene	10	10.	11.	36.	41.		(1)150.	*Condiments* (1)2.0		
2412 *ESTRAGON, OIL [*Artemisia dracunculus* L.]--Tarragon, oil	18	0.79	0.50 0.70	0.85	17.			*Alcoholic Beverages* 1.0 3.0	*Condiments* 26.	*Meats* (1)40.
2413 *p*-ETHOXYBENZALDEHYDE	2	0.06 0.08	0.36 0.50	1.0 1.0	1.0 1.0					
2414 ETHYL ACETATE--Acetic ether; Vinegar naphtha	81	67.	99.	170.	170.	200.	1,400.	*Alcoholic Beverages* 50. 65.		
2415 ETHYL ACETOACETATE--Acetoacetic ester; Ethyl 3-oxobutanoate	21	17.	24.	110.	120.	93.	530.			
2416 ETHYL 2-ACETYL-3-PHENYLPROPIONATE--Ethyl benzyl acetoacetate; Ethyl α-acetylhydrocinnamate	2	0.10 5.0	(1)2.0	(1)7.0	-					
2417 ETHYL ACONITATE (Mixed esters)--Ethyl 1-propene-1,2,3-tricarboxylate	5	3.6	12.	55.	66.	(1)2.5				
2418 ETHYL ACRYLATE	5	0.13 0.26	0.06 1.0	1.1	1.1		0.10 0.10			

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FEMA No. and Substance	No. of Reports	Beverages	Ice Cream, Ices, Etc.	Candy	Baked Goods	Gelatins and Puddings	Chewing Gum	—Other Category Uses—		
2419 ETHYL ALCOHOL--Ethanol	92	1,700.	2,000.	2,200.	1,800.	(1)230.	1,400.	Maple Syrup (1)610. Alcoholic Beverages 250. 450,000.	Condiments (1)1,000.	Dairy Products (1)30.
2420 ETHYL p-ANISATE	10	2.6	0.96	8.8	7.2					
2421 ETHYL ANTHRANILATE	21	5.9	7.6	19.	23.	14.	(1)79.			
2422 ETHYL BENZOATE--Ethyl benzenecarboxylate	31	2.8	2.8	9.0	10.	(1)0.06	59.	Alcoholic Beverages (1)0.50		
2423 ETHYL BENZOYLACETATE	1	(1)0.70	(1)5.0	(1)10.	(1)10.					
2424 α-ETHYL BENZYL BUTYRATE--α-Phenylpropyl butyrate	3	0.13 1.0	0.12 0.20	1.0	(1)0.14					
2425 2-ETHYL BUTYL ACETATE	2	(1)5.0	(1)2.0	0.03 7.0	-					
2426 2-ETHYLBUTYRALDEHYDE	2	(1)10.	(1)40.	0.12 25.	0.20 20.					
2427 ETHYL BUTYRATE	77	28.	44.	98.	93.	54.	1,400.			
2428 ETHYL iso-BUTYRATE	8	10.	25.	73.	(1)200.	(1)6.0		Toppings (1)1.5		
2429 2-ETHYLBUTYRIC ACID--α-Ethylbutyric acid	2	(1)5.0	(1)20.	20. 35.	(1)20.					
2430 ETHYL CINNAMATE--Ethyl 3-phenylpropenoate; Ethyl phenylacrylate	27	4.1	8.8	9.5	12.	2.4	11. 40.			
2431 ETHYL CYCLOHEXANEPROPIONATE--Ethyl cyclohexylpropionate	2	(1)9.0	-	0.03 30.	(1)24.	-				
2432 ETHYL DECANOATE	12	2.1	4.5	8.3	23.	5.3		Alcoholic Beverages 3.0 10.		
2433 ETHYLENE OXIDE[1]--Epoxyethane	6	-	-	-	-			Ground Spices 21.	Whole Spices 15. 45.	
2434 ETHYL FORMATE--Formic ether	49	9.4	21.	50.	98.	0.35 11.	430.	Alcoholic Beverages (1)10.		
2435 ETHYL 2-FURANPROPIONATE--Ethyl furylpropionate; Ethyl furfurylhydracrylate	8	1.6	1.6	5.6	7.5					
2436 4-ETHYLGUAIACOL--4-Ethyl-2-methoxyphenol	2	(1)0.05	(1)1.1	-	-	(1)0.23				
2437 ETHYL HEPTANOATE	39	6.8	7.5	17.	24.	0.06 350.	340.	Alcoholic Beverages 8.5 20.		
2438 2-ETHYL-2-HEPTENAL--2-Ethyl-3-butylacrolein	2	(1)0.40	-	0.03 2.0	-					
2439 ETHYL HEXANOATE--Capronic ether absolute	26	7.0	18.	12.	12.	(1)10.	32.	Jellies (1)1.8		
2440 ETHYL LACTATE--Ethyl α-hydroxypropionate	25	5.4	17.	28.	71.	8.3	580. 3,100.	Alcoholic Beverages (1)1,000.	Syrups (1)35.	
2441 ETHYL LAURATE--Ethyl dodecanoate	15	1.7	3.7	17.	17.	4.4	(1)39.	Alcoholic Beverages (1)3.0		
2442 ETHYL LEVULINATE	6	5.8	11.	12.	12.					
2443 ETHYL 2-METHYLBUTYRATE	1	(1)0.50	(1)3.0	(1)5.0	-					
2444 ETHYL METHYL PHENYLGLYCIDATE--Ethyl 3-methyl-3-phenylglycidate; Strawberry aldehyde; Aldehyde C-16 Pure (so-called)	58	5.6	6.7	21.	18.	13.	470.			
2445 ETHYL MYRISTATE--Ethyl tetradecanoate	7	6.7	8.0	10.	14.			Alcoholic Beverages (1)30.		

[1] As a fumigant for whole and ground spices, provided that residues of ethylene oxide do not exceed 50 p.p.m.

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2446 ETHYL NITRITE--Spirit of nitrous ether; Sweet spirit of nitre	11	3.0	4.5	0.10 8.0	(1)0.10		(1)3.9	*Icings* (1)13.	*Syrups* (1)52.	
2447 ETHYL NONANOATE	28	3.9	4.0	14.	15.	(1)15.	(1)580.	*Alcoholic Beverages* 20.	*Icings* (1)39.	
2448 ETHYL 2-NONYNOATE--Ethyl octyne carbonate	5	0.56	0.55	0.52	1.2					
2449 ETHYL OCTANOATE	16	4.1	2.4	9.0	11.	0.10 2.7	4.0 60.			
2450 ETHYL OLEATE	2	(1)0.10	(1)0.10	0.10 40.	0.10 55.	(1)0.10				
2451 ETHYL PALMITATE--Ethyl hexadecanoate	1	-	(1)20.	(1)40.	(1)20.					
2452 ETHYL PHENYLACETATE--α-Toluic acid, ethyl ester	14	2.4	5.2	8.1	6.0			*Syrups* (1)24.		
2453 ETHYL 4-PHENYLBUTYRATE	2	0.06 1.0	-	(1)0.06	-					
2454 ETHYL 3-PHENYLGLYCIDATE	17	4.6	12.	18.	20.	10. 70.				
2455 ETHYL 3-PHENYLPROPIONATE--Ethyl hydrocinnamate	5	1.8	1.0	2.5	0.50 3.0					
2456 ETHYL PROPIONATE	33	7.7	29.	78.	110.	10. 15.	1,100.			
2457 ETHYL PYRUVATE	4	(1)50.	20. 150.	35.	40.					
2458 ETHYL SALICYLATE--Salicylic ether; Sal ethyl	15	2.8	11.	10.	16.	(1)0.04	(1)16.			
2459 ETHYL SORBATE--Ethyl 2,4-hexadienoate	5	5.5	14.	15.	18.					
2460 ETHYL TIGLATE--Ethyl *trans*-2-methyl-2-butenoate	8	5.3	6.0	20.	6.5					
2461 ETHYL 10-UNDECENOATE	6	1.7	8.7	10.	11.			*Alcoholic Beverages* (1)5.0		
2462 ETHYL VALERATE	24	4.2	4.4	35.	8.3	5.5	260.			
2463 ETHYL *iso*-VALERATE--Ethyl β-methylbutyrate	33	4.9	7.8	29.	27.	5.0	80. 430.	*Condiments* (1)1.0		
2464 ETHYL VANILLIN--3-Ethoxy-4-hydroxybenzaldehyde; Ethovan; Vanillal	110	20.	47.	65.	63.	74.	110.	*Alcoholic Beverages* (1)100. *Chocolate* 250.	*Imitation Vanilla Extract* 28,000.	*Icings & Toppings* 140. 200.
2465 EUCALYPTOL--1,8-Epoxy-*p*-menthane; Cineole; Cajeputol	9	(1)0.13	(1)0.50	15.	0.50 4.0		190.			
2466 EUCALYPTUS OIL--*Eucalyptus globulus* Labille	14	1.7	0.50 50.	130.	76.			*Alcoholic Beverages* (1)1.0		
2467 EUGENOL--4-Allyl-2-methoxyphenol; 4-Allylguaiacol; 4-Hydroxy-3-methoxy-1-allylbenzene	36	1.4	3.1	32.	33.	(1)0.60	500.	*Condiments* 9.6 100.	*Meats* 40. 2,000.	
2468 *iso*-EUGENOL--2-Methoxy-4-propenylphenol; 4-Propenylguaiacol	15	3.7	3.8	5.0	11.		0.30 1,000.	*Condiments* (1)1.0		
2469 EUGENYL ACETATE--Acetyl eugenol	12	0.43	3.3	20.	10.		25. 100.	*Condiments* 2.0 2.0		
2470 *iso*-EUGENYL ACETATE--2-Methoxy-4-propenylphenyl acetate; Acetyl *iso*-eugenol	6	0.44	2.1	17.	17.		(1)100.			
2471 EUGENYL BENZOATE--4-Allyl-2-methoxyphenyl benzoate; Benzoyl eugenol	2	0.03 0.13	0.25 2.0	0.25 10.	0.13 10.					
2472 *iso*-EUGENYL ETHYL ETHER--2-Ethoxy-5-propenylanisole; Ethyl *iso*-eugenol	2	(1)7.8	(1)0.50	(1)17.	1.0 3.5					
2473 EUGENYL FORMATE--4-Allyl-2-methoxyphenyl formate	1	-	-	-	-			*Condiments* (1)0.20		

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2474 iso-EUGENYL FORMATE--2-Methoxy-4-propenylphenyl formate	1	•	•	•	•			*Condiments* (1)0.20		
2475 EUGENYL METHYL ETHER--4-Allylveratrole; Methyl eugenol; 1,2-Dimethoxy-4-allylbenzene	8	10.	4.8	11.	13.			*Jellies* (1)52.		
2476 *iso*-EUGENYL METHYL ETHER--4-Propenylveratrole, Methyl *iso*-eugenol	10	4.0	7.7	13.	18.	(1)0.10	(1)110.			
2477 *iso*-EUGENYL PHENYLACETATE--2-Methoxy-4-propenylphenyl phenylacetate	2	(1)0.05	(1)0.20	(1)3.0	2.0 3.0					
2478 FARNESOL--3,7,11-Trimethyl-2,6-10-dodecatrien-1-ol	7	0.76	0.40	1.4	1.7	(1)0.10				
2479 *d*-FENCHONE--*d*-1,3,3-Trimethyl-2-norbornanone	4	0.13 0.80	(1)0.25	0.25 30.	(1)0.25			*Alcoholic Beverages* (1)5.0		
2480 FENCHYL ALCOHOL--1,3,3-Trimethyl-2-norbornanol; 2-Fenchanol; Fenchol	3	1.8	(1)0.25	4.7	(1)0.25					
2481 *FENNEL, COMMON--*Foeniculum vulgare* Mill.	9	(1)800.	•	•	300. 6,500.			*Condiments* (1)50.	*Meats* 2,400.	
2482 *FENNEL, SWEET [*Foeniculum vulgare* Mill. var. *dulce* (DC.) Alef.]--Finochio; Florence fennel	4	(1)11.	(1)44.	(1)33.	(1)33.			*Meats* 40. 300.		
2483 *FENNEL, SWEET, OIL--*Foeniculum vulgare* Mill. var. *dulce* (DC.) Alef.	31	3.9	0.38	22.	19.	0.10 10.		*Alcoholic Beverages* 10. 20.	*Condiments* (1)2.0	*Meats* 40. 100.
2484 *FENUGREEK--*Trigonella foenum-graecum* L.	13	(1)470.	15. 560.	600.	570.			*Condiments* 420. 800.	*Meats* (1)250.	*Syrups* (1)450.
2485 *FENUGREEK, EXTRACT--*Trigonella foenum-graecum* L.	51	50.	45.	280.	99.	30.	(1)7.6	*Alcoholic Beverages* (1)20. *Pickles* (1)90.	*Condiments* (1)150. *Syrups* 170.	*Icings* 37. *Meats* 40. 60.
2486 *FENUGREEK, OLEORESIN--*Trigonella foenum-graecum* L.	18	290.	72.	90.	72.	(1)500.		*Syrups* 300.		
2487 FORMIC ACID	2	(1)1.0	(1)5.0	5.0 18.	5.0 6.1					
2488 FUMARIC ACID--*trans*-Butenedioic acid; *trans*-1,2-Ethylenedicarboxylic acid; Allomaleic acid; Boletic acid	3	(1)50.	•	-	(1)1,300.	(1)3,600.				
2489 FURFURAL--2-Furaldehyde; Pyromucic aldehyde	16	4.0	13.	12.	17.	(1)0.80	45.	*Alcoholic Beverages* (1)10.	*Syrups* (1)30.	
2490 FURFURYL ACETATE	4	11.	17.	37.	1.0 40.		(1)500.			
2491 FURFURYL ALCOHOL--2-Furancarbinol; α-Furylcarbinol; 2-Furylcarbinol; 2-Hydroxymethylfuran; Furfuralcohol	5	19.	88.	59.	110.			*Alcoholic Beverages* (1)10.		
2492 2-FURFURYLIDENE BUTYRALDEHYDE--2-Ethyl-3-furylacrolein	2	(1)0.30	0.50 3.0	2.0 6.0	2.0 6.0					
2493 FURFURYL MERCAPTAN--2-Furanmethanethiol	18	0.52	0.78	2.0	2.1	(1)0.10		*Icings* (1)0.50		
2494 FURYL ACROLEIN--2-Furanacrolein	6	(1)0.17	6.1	36.	21.	0.10 0.56				
2495 4-(2-FURYL)-3-BUTEN-2-ONE--Furfurylidene acetone; Furfuralacetone	4	4.2	4.8	33.	46.	(1)1.6				
2496 (2-FURYL)-2-PROPANONE--Furyl acetone	3	•	(1)5.0	3.8 20.	2.0 20.					
2497 FUSEL, OIL, REFINED † --Amyl alcohol, commercial	20	21.	4.1	30.	34.	(1)4.0	(1)270.	*Alcoholic Beverages* (1)2.5		
2498 *GALANGAL ROOT--*Alpinia officinarum* Hance; *A. galanga* Willd.	4	750.	•	•	•					

† Assuming that refined fusel oil is mixed amyl alcohols, predominantly 3-Methyl-1-butanol

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2499 •GALANGAL ROOT, EXTRACT—*Alpinia officinarum* Hance, *A. galanga* Willd.	5	0.10 350.	(1)0.30	(1)0.20	(1)0.10			*Alcoholic Beverages* (1)350.	*Bitters* (1)80.	
2500 •GALANGAL ROOT, OIL—*Alpinia officinarum* Hance, *A. galanga* Willd.	6	0.27	0.40	1.5	2.3			*Alcoholic Beverages* (1)1.0	*Condiments* (1)2.0	
2501 GALBANUM, OIL—*Ferula galbaniflua* Boiss. et Buhse and other *Ferula* spp.	5	0.16	0.84	1.7	1.8					
2502 GALBANUM, RESIN—*Ferula galbaniflua* Boiss. et Buhse and other *Ferula* spp.	5	0.04 0.25	0.05 0.50	1.7	2.4			*Condiments* (1)50.		
2503 •GARLIC, OIL—*Allium sativum* L.	20	0.01 0.30	(1)0.04	2.9	6.0		(1)12.	*Condiments* 16.		
2504 GENET, ABSOLUTE—*Spartium junceum* L.	5	0.83	0.50 1.0	1.7	1.0 2.0		(1)12.			
2505 GENET, EXTRACT [*Spartium junceum* L.]—Broom, extract	4	1.4	•	•	•					
2506 GENTIAN ROOT, EXTRACT—*Gentiana lutea* L.	22	26.	47.	120.	160.			*Alcoholic Beverages* 13.		
2507 GERANIOL—*trans*-3,7-Dimethyl-2,6-octadien-1-ol	36	2.1	3.3	10.	11.	2.0 2.0	0.80 2.9	*Toppings* (1)1.0		
2508 •GERANIUM, ROSE, OIL—*Pelargonium graveolens* L'Her.	36	1.6	2.8	6.9	8.1	1.4 2.0	(1)210.	*Jellies* (1)5.2		
2509 GERANYL ACETATE	37	1.6	6.5	15.	17.	6.8 7.5	0.30 1.2	*Syrups* (1)1.0		
2510 GERANYL ACETOACETATE	2	0.50 0.50	1.0 1.0	1.0 3.0	1.0 10.					
2511 GERANYL BENZOATE	3	0.10 0.13	0.16 0.25	(1)0.50	(1)0.50					
2512 GERANYL BUTYRATE	17	1.6	2.8	10.	10.	5.3	0.30 1.5			
2513 GERANYL *iso*-BUTYRATE	8	1.0	0.80	5.0	4.9	(1)0.60	(1)15.			
2514 GERANYL FORMATE	17	1.9	1.6	7.5	4.1	3.4	(1)0.80			
2515 GERANYL HEXANOATE	8	1.3	0.90	3.2	(1)2.0					
2516 GERANYL PHENYLACETATE	10	1.1	3.1	6.7	4.7		(1)11.			
2517 GERANYL PROPIONATE	12	1.5	1.3	3.7	4.9	(1)3.0	30. 70.			
2518 GERANYL *iso*-VALERATE	9	4.2	11.	10.	6.8					
2519 •GHATTI, GUM [*Anogeissus latifolia* Wall.]—Indian gum	4	(1)2,100.	(1)800.	•	•					
2520 •GINGER—*Zingiber officinale* Rosc.	40	44.	220.	•	2,500.			*Meats* 1,500.		
2521 •GINGER, EXTRACT—*Zingiber officinale* Rosc.	32	65.	43.	83.	100.			*Condiments* (1)15.	*Meats* 56.	
2522 •GINGER, OIL—*Zingiber officinale* Rosc.	52	17.	20.	14.	47.			*Condiments* 13.	*Meats* 12.	
2523 •GINGER, OLEORESIN—*Zingiber officinale* Rosc.	43	79.	36. 65.	27.	52.			*Condiments* 10. 1,000.	*Meats* 30. 250.	
2524 GLUCOSE PENTAACETATE	1	(1)100.	•	•	(1)1,500.					
2525 GLYCEROL—Glycerine; 1,2,3-Propanetriol trihydroxypropane	53	570.	500.	980.	1,300.	(1)360.	17. 6,000.	*Extracts* (1)400,000.	*Meats* (1)40.	*Toppings* (1)23,000.
2526 GLYCERYL MONOOLEATE—(mono)Olein	4	(1)15.	•	(1)8.0	30. 2,000.			*Shortening* (1)600.		
2527 GLYCERYL MONOSTEARATE—(mono)Stearin; Glyceryl monooctadecanoate	6	•	2,000.	(1)100.	1,100.		(1)1,600.			

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2528 GLYCYRRHIZIN, AMMONIATED--*Glycyrrhiza glabra* L. and other spp. of *Glycyrrhiza*	15	51.	•	5.0 62.	(1)5.0			
2529 *GRAINS OF PARADISE--*Aframomum melegueta* (Rosc.)K. Schum.	6	43.	(1)120.	(1)120.	•			
2530 *GRAPEFRUIT, OIL--*Citrus paradisi* Macf.	53	160.	180.	630.	370.	(1)250.	1,500.	*Toppings* (1)400.
2531 GUAIAC GUM, EXTRACT--*Guaiacum officinale* L.; *G. sanctum* L.	2	(1)600.	•	•	•			
2532 GUAIACOL--o-Methoxyphenol; o-Hydroxyanisole; Methylcatechol	11	0.95	0.52	0.96	0.75			
2533 GUAIAC WOOD, EXTRACT--*Guaiacum officinale* L.; *G. sanctum* L.; *Bulnesia sarmienti* Lorentz	6	760.	(1)4.0	(1)8.0	(1)70.			
2534 GUAIAC WOOD, OIL--*Guaiacum officinale* L.; *G. sanctum* L.; *Bulnesia sarmienti* Lorentz	25	1.1	4.1	9.2	8.1	4.2	(1)60.	
2535 GUAIACYL PHENYLACETATE	4	0.38	1.0	2.2	3.2			*Toppings* (1)1.0
2536 GUARANA, GUM--*Paullinia cupana* HBK.	7	12.	•	(1)10.	•			
2537 GUAR, GUM [*Cyamopsis tetragonolobus* (L.) Taub.]--Guar flour; Gum cyamopsis; Jaguar; Regonol; Burtonite V-7-E	8	47. 100.	(1)5,000.	(1)10.	(1)2,900.			*Meats* (1)2,500.
2538 HAW BARK, BLACK, EXTRACT--*Viburnum prunifolium* L.	5	5.0 6.0	(1)2.5	(1)6.0	(1)6.0			
3034 HEMLOCK, OIL (See SPRUCE, OIL)-- *Tsuga canadensis* (L.) Carr.; *T. heterophylla* (Raf.) Sarg.; *Picea mariana* (Mill.); *P. glauca* (Moench) Voss								
2539 γ-HEPTALACTONE--4-Hydroxyheptanoic acid, γ-lactone	4	18.	40.	28.	26.			
2540 HEPTANAL--Enanthaldehyde; Heptaldehyde; Heptyl aldehyde; Enanthol; Aldehyde C-7	10	4.9	1.2	2.0	2.6			*Alcoholic Beverages* (1)4.0
2541 HEPTANAL DIMETHYL ACETAL	3	•0.10 0.13	(1)0.25	(1)0.25	(1)0.25			*Condiments* (1)1.0
2542 HEPTANAL GLYCERYL ACETAL (Mixed 1,2 and 1,3 acetals)	2	(1)5.0	(1)10.	(1)10.	(1)10.			*Condiments* (1)100.
2543 2,3-HEPTANEDIONE--Acetyl valeryl; Acetyl pentanoyl	14	0.86	3.1	8.2	7.9		(1)1.7	
2544 2-HEPTANONE--Methyl amyl ketone; Ketone C-7	11	2.7	6.0	6.4	13.			*Condiments* 10. 25.
2545 3-HEPTANONE--Ethyl butyl ketone	8	0.13 2.0	0.25 170.	67.	0.25 130.			
2546 4-HEPTANONE--Dipropyl ketone; Butyrone	8	7.4	11.	19.	27.	0.60 8.0		
2547 HEPTYL ACETATE	6	4.1	3.3	4.9	4.8			
2548 HEPTYL ALCOHOL--1-Heptanol; Enanthyl alcohol; n-Heptyl alcohol; Hydroxyheptane; Enanthic alcohol; Alcohol C-7	3	0.90	1.0 5.0	3.0	3.0			
2549 HEPTYL BUTYRATE	6	0.66	0.74	2.7	2.4			
2550 HEPTYL iso-BUTYRATE	5	1.2	0.82	2.6	3.0			
2551 HEPTYL CINNAMATE	4	3.3	1.0 2.0	1.0 6.0	(1)1.0		(1)270.	
2552 HEPTYL FORMATE	5	1.7	0.87	3.6	3.3			

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2553 HEPTYL OCTANOATE	1	(1)1.0	-	-	-					
2554 1-HEXADECANOL--Cetyl alcohol; Alcohol C-16	1	-	(1)2.0	(1)2.0	-					
2555 ω-6-HEXADECENLACTONE--16-Hydroxy-6-hexadecenoic acid, ω-lactone; 6-Hexadecenolide; Ambrettolide	6	0.32	0.18	0.16	0.19	(1)0.007	(1)0.70			
2556 γ-HEXALACTONE--4-Hydroxyhexanoic acid, γ-lactone; Ethyl butyrolactone; Tonkalide	3	7.0	0.07 84.	21.	21.					
2557 HEXANAL--Hexaldehyde; Hexoic aldehyde; Caproic aldehyde; Caproaldehyde	10	1.3	2.8	3.6	4.2	2.0 2.5	(1)3.0			
2558 2,3-HEXANEDIONE--Acetyl butyryl	8	6.6	4.8	7.3	6.6					
2559 HEXANOIC ACID--Caproic acid; Hexoic acid	30	1.8	4.3	28.	22.		(1)1.5	Condiments (1)450.		
2560 2-HEXENAL	8	3.1	0.70	15.	16.					
2561 cis-3-HEXENAL	1	(1)0.20	(1)5.0	(1)5.0	-					
2562 2-HEXEN-1-OL	7	1.0	0.63	3.8	4.1					
2563 3-HEXEN-1-OL--Leaf alcohol; Blätteralkohol	6	1.0	3.7	5.0	5.0					
2564 2-HEXEN-1-YL ACETATE	4	0.28	0.40	1.7	1.7					
2565 HEXYL ACETATE	10	4.6	4.6	26.	26.		(1)3.0			
2566 2-HEXYL-4-ACETOXYTETRAHYDROFURAN	1	(1)1.0	(1)3.0	(1)3.0	(1)3.0					
2567 HEXYL ALCOHOL--1-Hexanol	10	6.6	26.	21.	18.	0.22 0.28				
2568 HEXYL BUTYRATE	6	2.6	2.1	7.8	8.6					
2569 α-HEXYLCINNAMALDEHYDE	8	0.80	2.6	6.5	2.4	(1)0.05				
2570 HEXYL FORMATE	5	12.	45.	39.	52.					
2571 HEXYL 2-FUROATE	2	-	-	(1)0.31	-			Condiments (1)0.20		
2572 HEXYL HEXANOATE	3	2.5 3.0	(1)2.5	3.6 10.	(1)10.					
2573 2-HEXYLIDENE CYCLOPENTANONE	1	(1)1.0	(1)5.0	(1)10.	-					
2574 2-HEXYL-5 or 6-KETO-1,4-DIOXANE--(1 or 2-Hexyl-2-hydroxyethoxy)acetic acid, δ-lactone	1	-	(1)5.0	(1)5.0	(1)5.0			Margarine (1)5.0		
2575 HEXYL OCTANOATE	2	(1)1.0	-	-	-	(1)0.70				
2576 HEXYL PROPIONATE	5	5.7	23.	21.	22.					
2577 *HICKORY BARK, EXTRACT--*Carya* spp.	5	21. 40.	0.01 25.	(1)48.	(1)48.			Alcoholic Beverages (1)70.	Condiments 65.	
2578 *HOPS, EXTRACT--*Humulus lupulus* L.	5	160.	-	-	-					
2579 *HOPS, EXTRACT SOLID--*Humulus lupulus* L.	4	8.0	20. 75.	0.70 50.	0.80 40.					
2580 *HOPS, OIL--*Humulus lupulus* L.	13	1.7	1.7	2.5	2.9		(1)2.2	Condiments 20. 35.		
2581 *HOREHOUND (HOARHOUND), EXTRACT--*Marrubium vulgare* L.	10	8.7	(1)2.0	680.	(1)2.0					
2582 *HORSEMINT LEAVES, EXTRACT--*Monarda* spp.	2	(1)600.	-	-	-					

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83 ... DROXYCITRONELLAL--3,7-Dimethyl-7-hydroxy-octanal, Launne ®	17	3.5	13.	9.4	10.	(1)0.30	16.			
2584 HYDROXYCITRONELLAL DIETHYL ACETAL	4	2.7	0.50 1.0	7.3	2.2					
2585 HYDROXYCITRONELLAL DIMETHYL ACETAL	4	10.	(1)0.50	24.	0.50 20.					
2586 HYDROXYCITRONELLOL--3,7-Dimethyl-1,7-octanediol	9	2.0	1.6	3.6	3.5	(1)0.30	(1)0.30			
2587 5-HYDROXY-4-OCTANONE--Butyroin	6	0.50 5.0	1.0 20.	10.	7.8					
2588 4-(p-HYDROXYPHENYL)-2-BUTANONE--p-Hydroxybenzyl acetone	9	16.	34.	44.	84.	5.0 50.	40. 320.			
2589 *HYSSOP--*Hyssopus officinalis* L.	2	•	•	•	•			*Bitters* (1)600.		
2590 *HYSSOP, EXTRACT--*Hyssopus officinalis* L.	2	(1)13.	(1)13.	•	•			*Alcoholic Beverages* (1)50.		
2591 *HYSSOP, OIL--*Hyssopus officinalis* L.	6	4.7	(1)0.25	14.	0.25 33.			*Alcoholic Beverages* 5.0 50.		
2592 *IMMORTELLE, EXTRACT--*Helichrysum angustifolium* DC.	7	5.2	16.	11.	15.	(1)0.01	(1)0.50			
2593 INDOLE--2,3-Benzopyrrole	18	0.26	0.28	0.50	0.58	0.02 0.40				
2594 α-IONONE—4-(2,6,6-Trimethyl-2-cyclohexen-1-yl)-3-buten-2-one; α-Irisone ®	33	2.5	3.6	12.	6.7	3.6	39.	*Icings* (1)50.		
2595 'ONONE—4-(2,6,6-Trimethyl-1-cyclohexen-1-yl)-3-buten-2-one; β-Irisone ®	35	1.6	3.4	7.6	5.2	5.8	89.	*Maraschino Cherries* (1)10.		
2596 *IRISH MOSS, EXTRACT [*Chondrus crispus* (L.) Stackh. or *Gigartina mamillosa* (Goodex. et Woodw.) J. Ag.]--Carrageen, extract; Chondrus, extract	24	300.	390.	3.0 500.	1,300.	1,700. 20,000.		*Jellies* (1)200.	*Syrups* 1,300.	
2597 α-IRONE--4-(2,5,6,6-Tetramethyl-2-cyclohexen-1-yl)-3-buten-2-one; 6-Methylionone	13	1.2	2.3	4.1	5.4		(1)1.4			
2598 *JASMINE, ABSOLUTE—*Jasminum grandiflorum* L.	15	0.41	1.3	0.80	2.9	0.10 0.50	(1)30.			
2599 *JASMINE, CONCRETE—*Jasminum grandiflorum* L.	5	0.70	1.0 1.5	1.0 3.4	1.0 15.	(1)1.0				
2600 *JASMINE, OIL--*Jasminum grandiflorum* L.	13	0.63	1.6	3.0	9.3	0.50 1.0	(1)1.4	*Jellies* (1)0.25		
2601 *JASMINE, SPIRITUS—*Jasminum grandiflorum* L.	3	(1)1.0	(1)0.75	(1)3.0	(1)4.0	(1)1.0		*Maraschino Cherries* (1)10.		
2602 *JUNIPER BERRIES--*Juniperus communis* L.	3	•	•	•	•			*Condiments* (1)60.	*Alcoholic Beverages* 60. 2,000.	
2603 *JUNIPER, EXTRACT—*Juniperus communis* L.	4	53.	(1)5.0	(1)5.0	(1)5.0					
2604 *JUNIPER, OIL--*Juniperus communis* L.	25	32.	1.9	4.3	11.	(1)0.01	(1)0.10	*Alcoholic Beverages* 95.	*Meats* (1)20.	
2605 *KARAYA, GUM [*Sterculia urens* Roxb.]--Sterculia; Indian tragacanth, Kadaya, Kullo, Kattilo; Mucara; Kuteera]	20	13.	1,300.	1.0 44.	36.			*Emulsions* 20. 18,000.	*Meats* (1)40.	*Toppings* (1)3,500.
2606 *KELP--Atlantic: *Laminaria digitata; L. saccharina;* Pacific: *Macrocystis pyrifera* (L.) C. Agardh	1	•	•	•	•					
2607 *KOLA NUT, EXTRACT--*Cola acuminata* Schott et Endl.	34	120.	220.	160.	150.					
2608 LABDANUM, ABSOLUTE--*Cistus* spp.	8	2.8	9.8	5.6	23.	(1)0.06	1.0 19.			
2609 LABDANUM, OIL [*Cistus* spp.]--Ambreine, oil	5	0.41	0.78	2.0	0.75					
2610 LABDANUM, OLEORESIN--*Cistus* spp.	6	2.7	(1)2.0	5.5	(1)4.0					

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FEMA No. and Substance	No. of Reports	Beverages	Ice Cream, Ices, Etc.	Candy	Baked Goods	Gelatins and Puddings	Chewing Gum	— Other Category Uses —		
2611 LACTIC ACID	25	34.	66.	130.	89.	14. 25.	(1)610.	*Pickles & Olives* 1,200. 24,000.	*Toppings* (1)300.	
2612 *LAUREL BERRIES--*Laurus nobilis* L.	2	(1)450.	-	-	-					
2613 *LAUREL LEAVES, EXTRACT--*Laurus nobilis* L.	1	-	-	-	-			*Spiced Vegetables* (1)5.0		
2614 LAURIC ACID--Dodecanoic acid; Laurostearic acid; Dodecoic acid	1	(1)15.	(1)16.	(1)2.4	(1)39.	(1)25.				
2615 LAURIC ALDEHYDE--Dodecanal; Lauraldehyde; Aldehyde C-12 Lauric	21	0.93	1.5	2.4	2.8	(1)0.10	0.20 110.			
2616 LAURYL ACETATE--Dodecyl acetate; Dodecanyl acetate; Acetate C-12	9	2.3	1.7	4.6	5.6					
2617 LAURYL ALCOHOL--Dodecyl alcohol; 1-Dodecanol; Alcohol C-12	11	2.0	1.0	2.8	1.7		16. 27.	*Syrups* (1)7.0		
2618 *LAVANDIN, OIL--Hybrids between *Lavandula officinalis* Chaix and *L. latifolia* Vill.	5	5.5	12.	18.	18.		(1)0.30			
2619 *LAVENDER--*Lavandula officinalis* Chaix	1	(1)0.08	-	-	-					
2620 *LAVENDER, ABSOLUTE--*Lavandula officinalis* Chaix	2	0.20 7.5	(1)0.40	2.0 14.	2.0 6.3					
2621 *LAVENDER, CONCRETE--*Lavandula officinalis* Chaix	2	0.01 0.20	(1)0.08	0.03 0.25	(1)0.25					
2622 *LAVENDER, OIL--*Lavandula officinalis* Chaix	8	2.9	7.8	5.5	8.3		(1)220.			
2623 *LEMON, EXTRACT--*Citrus limon* (L.) Burm. f.	12	1,000.	540. 4,000.	400. 12,000.	8,900.			*Icings* (1)10,000.		
2624 *LEMON-GRASS, OIL--*Cymbopogon citratus* DC. and *C. flexuosus* Stapf	9	4.4	9.2	38.	38.	(1)290.	(1)220.			
2625 *LEMON, OIL--*Citrus limon* (L.) Burm. f.	120	230.	380.	1,100.	580.	340.	1,900.	*Breakfast Cereals* (1)140. *Meats* 25. 40.	*Condiments* 10. 80. *Syrups* (1)65.	*Icings* 65. 600.
2626 *LEMON, OIL, TERPENELESS [*Citrus limon* (L.) Burm. f.]--Cedro, oil	64	13.	25.	68.	50.	80.	110. 670.	*Toppings* (1)1,000.		
2627 LEVULINIC ACID--3-Acetylpropionic acid; 4-Oxovaleric acid	3	14.	14.	53.	53.	(1)4.0				
2628 *LICORICE, EXTRACT [*Glycyrrhiza glabra* L. and other spp. of *Glycyrrhiza*]--Glycyrrhiza, extract	38	33.	39.	130.	84.	(1)4.0	(1)29,000.	*Syrups* (1)50.		
2629 *LICORICE, EXTRACT POWDER--*Glycyrrhiza glabra* L.	7	110.	(1)200.	6,500.	(1)200.		22,000. 22,000.			
2630 *LICORICE ROOT [*Glycyrrhiza glabra* L.]--Glycyrrhiza	13	130.	-	(1)460.	(1)75.		(1)3,200.			
2631 *LIME, OIL--*Citrus aurantifolia* (Christman) Swingle	97	130.	160.	680.	370.	200.	3,100.	*Condiments* (1)20.		
2632 *LIME, OIL, TERPENELESS--*Citrus aurantifolia* (Christman) Swingle	42	15.	17.	37.	22.	26.	(1)0.10	*Syrups* (1)8.0		
2633 *d*-LIMONENE--*d*-*p*-Mentha-1,8-diene; Cinene; Dipentene; Cajeputene; Kautschin	14	31.	68.	49.	120.	48. 400.	2,300.			
2634 LINALOE WOOD, OIL--*Bursera delpechiana* Poiss. and other *Bursera* spp.	10	4.3	3.8	16.	15.			*Alcoholic Beverages* (1)1.0		
2635 LINALOÖL--3,7-Dimethyl-1,6-octadien-3-ol; Linalol; Licareol	35	2.0	3.6	8.4	9.6	2.3	0.80 90.	*Meats* (1)40.		

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2636 LINALYL ACETATE--Bergamol	29	1.9	3.8	11.	8.9	3.8	13.			
2637 LINALYL ANTHRANILATE	8	1.8	0.72	4.7	0.20 8.0					
2638 LINALYL BENZOATE	5	0.31	0.42	1.2	1.6	(1)0.28				
2639 LINALYL BUTYRATE	13	1.2	4.3	2.2	13.	(1)0.09				
2640 LINALYL *iso*-BUTYRATE	12	1.7	2.8	4.9	13.					
2641 LINALYL CINNAMATE	6	0.57	0.59	2.0	2.1					
2642 LINALYL FORMATE	11	1.3	12.	3.8	13.		(1)1.2			
2643 LINALYL HEXANOATE	3	3.2	6.0	11.	(1)15.					
2644 LINALYL OCTANOATE	3	1.3	0.50 3.0	0.50	0.60 15.					
2645 LINALYL PROPIONATE	11	4.9	3.6	5.3	12.	(1)4.4				
2646 LINALYL *iso*-VALERATE	13	0.96	0.91	5.7	5.6	(1)0.10				
2647 *LINDEN FLOWERS--*Tilia glabra* Vent.	5	12. 2,000.	-	-	-					
2648 *LOCUST, GUM--*Ceratonia silique* L.	21	2,900.	1,200.	-	(1)150.			*Condiments* (1)980.	*Toppings* 1,500. 6,000.	
2649 LOVAGE [*Levisticum officinale* Koch]--Smallage; Smellage	11	4.0 30.	18.	28.	25.			*Syrups* (1)0.08		
2650 LOVAGE, EXTRACT [*Levisticum officinale* Koch]--Smellage, extract; Smallage, extract	20	8.8	18.	26.	24.			*Condiments* (1)40.	*Icings* (1)0.07	*Syrups* 66.
2651 LOVAGE, OIL [*Levisticum officinale* Koch]--Smellage, oil; Smallage, oil	26	1.3	0.60	0.83	2.4			*Condiments* 3.7	*Icings* (1)10.	*Syrups* 6.8
2652 *MACE--*Myristica fragrans* Houtt.	28	330.	(1)40.	-	1,300.			*Condiments* 43.	*Meats* 500. 2,000.	
2653 *MACE, OIL--*Myristica fragrans* Houtt.	45	6.0	4.5	23.	68.		(1)37.	*Condiments* 12.	*Meats* 33.	
2654 *MACE, OLEORESIN--*Myristica fragrans* Houtt.	7	-	-	-	360.			*Condiments* (1)800.	*Meats* 100. 600.	*Pickles* (1)35.
2655 *l*-MALIC ACID--*l*-Hydroxysuccinic acid; Apple acid	10	380.	390.	420.	0.60 1.5					
2656 MALTOL--3-Hydroxy-2-methyl-4*H*-pyran-4-one; 3-Hydroxy-2-methyl-γ-pyrone; Larixinic acid; Corps Praline; Palatone	23	4.1	8.7	31.	30.	7.5	90.	*Jellies* (1)15.		
2657 *MANDARIN, OIL--*Citrus reticulata* Blanco	44	62.	160.	350.	190.	(1)30.	83.			
2658 *MARIGOLD, POT [*Calendula officinalis* L.]--Calendula	1	(1)11.	(1)44.	(1)33.	(1)33.					
2659 *MARJORAM, OLEORESIN--*Majorana hortensis* Moench (*Origanum majorana* L.)	7	-	-	-	-			*Condiments* (1)75.	*Meats* 37.	
2660 *MARJORAM, POT--*Origanum vulgare* L.	0	-	-	-	-					
2661 *MARJORAM SEED--*Majorana hortensis* Moench (*Origanum majorana* L.)	7	(1)750.	-	-	-			*Condiments* 70. 700.	*Meats* 200. 3,500.	
2662 MARJORAM, SWEET--*Majorana hortensis* Moench (*Origanum majorana* L.)	23	(1)1.9	-	-	2,000.			*Condiments* (1)200.	*Meats* 510.	*Soups* (1)150.
2663 *MARJORAM, SWEET, OIL--*Majorana hortensis* Moench (*Origanum majorana* L.)	23	4.2	1.0	4.0	15.			*Condiments* 8.0		

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2664 p-MENTHA-1,8-DIEN-7-OL--Perillyl alcohol; 1-Hydroxymethyl-4-iso-propenyl-1-cyclohexene	3	0.50 1.0	0.50 1.0	20.	10. 50.				
2665 MENTHOL--5-Methyl-2-iso-propylcyclohexanol; Hexahydrothymol; 3-p-Menthanol; 5-Methyl-2-iso-propyl hexahydrophenol; l-Menthol; Peppermint camphor	31	35.	68.	400.	130.		1,100.		
2666 (d)-neo-MENTHOL--2-iso-Butyl-5-methyl cyclohexanol	4	10.	31.	50.	48.				
2667 MENTHONE--p-Menthan-3-one	10	7.7	33.	71.	52.		(1)8.7		
2668 MENTHYL ACETATE--p-Menth-3-yl acetate	9	5.5	4.0	26.	24.		(1)5.2		
2669 MENTHYL iso-VALERATE--p-Menth-3-yl iso-valerate; Validol	8	5.0	2.9	7.4	18.				
2670 p-METHOXYBENZALDEHYDE--p-Anisaldehyde; Aubepine liquid	32	6.3	5.6	14.	16.	0.50 30.	18. 76.		
2671 2-METHOXY-4-METHYLPHENOL--4-Methylguaiacol; 2-Methoxy-p-cresol; 4-Hydroxy-3-methyl-1-methylbenzene; Creosol	6	10. 21.	0.05	0.77	1.0			Alcoholic Beverages (1)0.02	
2672 4-(p-METHOXYPHENYL)-2-BUTANONE--Anisyl acetone	4	12.	10. 12.	28.	26.	(1)25.			
2673 1-(p-METHOXYPHENYL)-1-PENTEN-3-ONE--α-Methyl anisylidene acetone; Ethone	8	2.3	2.3	28.	12.				
2674 1-(p-METHOXYPHENYL)-2-PROPANONE--Anisyl methyl ketone; Anisic ketone; p-Methoxyphenyl acetone	2	0.60 2.8	1.2 2.8	4.4 6.0	4.4 6.0				
2675 2-METHOXY-4-VINYLPHENOL--p-Vinylguaiacol; 4-Hydroxy-3-methoxystyrene	2	0.25 3.0	0.25 11.	1.0 8.0	1.0 8.0				
2676 METHYL ACETATE	4	28.	29.	11.	14.	(1)0.10		Alcoholic Beverages (1)0.20	
2677 4'-METHYL ACETOPHENONE--Methyl p-tolyl ketone; p-Methyl acetophenone; p-Acetyl toluene; 1-Methyl-4-acetyl benzene	18	1.1	1.6	5.2	4.9		(1)870.	Maraschino Cherries (1)8.0	Condiments (1)5.8
2678 2-METHYLALLYL BUTYRATE--2-Methyl-2-propen-1-yl butyrate	2	(1)0.20	-	-	(1)0.20				
2679 METHYL ANISATE	7	2.7	3.0	8.0	6.2				
2680 o-METHYLANISOLE--o-Cresyl methyl ether; Methyl o-tolyl ether; 2-Methoxytoluene	3	1.7	(1)1.0	2.3 4.0	(1)4.0				
2681 p-METHYLANISOLE--p-Cresyl methyl ether; p-Methoxytoluene; 4-Methoxytoluene	19	2.7	2.7	4.8	7.6	0.50 4.0		Condiments (1)2.0	Syrups (1)8.0
2682 METHYL ANTHRANILATE--o-Aminomethyl benzoate; Methyl 2-aminobenzoate	67	16.	21.	56.	20.	23.	2,200.	Alcoholic Beverages (1)0.20	
2683 METHYL BENZOATE--Oil of Niobe	15	2.2	4.5	8.4	9.9		(1)61.		
2684 α-METHYLBENZYL ACETATE--Styralyl acetate; Methyl phenylcarbinyl acetate; Styrolene acetate; Gardenol	11	3.9	5.4	12.	17.		(1)0.80	Toppings (1)30.	
2685 α-METHYLBENZYL ALCOHOL--Styralyl alcohol; 1-Phenylethanol; α-Phenylethyl alcohol; Methyl phenylcarbinol	6	4.6	3.8	6.8	9.0	(1)4.0	(1)0.30		
2686 α-METHYLBENZYL BUTYRATE--Styralyl butyrate; Methyl phenylcarbinyl butyrate	2	4.0 5.0	4.0 10.	10. 20.	10. 20.				

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2687 α-METHYLBENZYL *iso*-BUTYRATE--Styralyl *iso*-butyrate; Methyl phenylcarbinyl *iso*-butyrate	1	(1)2.0	(1)10.	(1)10.	(1)10.			
2688 α-METHYLBENZYL FORMATE--Styralyl formate; Methyl phenylcarbinyl formate	2	2.0 5.0	3.0 5.0	10. 20.	10. 20.			
2689 α-METHYLBENZYL PROPIONATE--Styralyl propionate; Methyl phenylcarbinyl propionate	2	4.0 5.0	4.0 5.0	10. 15.	10. 15.			
2690 METHYL *p-tert*-BUTYLPHENYLACETATE	3	(1)0.50	0.35 1.0	2.0	2.0			
2691 2-METHYLBUTYRALDEHYDE--2-Methylbutanal; Methyl ethyl acetaldehyde	3	1.5 2.0	2.0 8.0	6.6	5.7			
2692 3-METHYLBUTYRALDEHYDE--*iso*-Valeraldehyde; *iso*-Pentaldehyde; 3-Methylbutanal; *iso*-Valeric aldehyde; *iso*-Amyl aldehyde; *iso*-Valeral	10	0.63	1.4	2.8	3.1	(1)3.0		
2693 METHYL BUTYRATE	4	17.	31.	86.	48. 200.			
2694 METHYL *iso*-BUTYRATE	3	22.	38.	48. 200.	48. 200.			
2695 2-METHYLBUTYRIC ACID	1	(1)0.50	(1)3.0	(1)5.0				
2696 METHYL CELLULOSE--Cellulose methyl ether	5	90.	0.50 1,700.	0.50 30.	(1)0.65			*Toppings* (1)3,000.
2697 α-METHYLCINNAMALDEHYDE	4	0.50 11.	1.0 15.	26.	27.		(1)430.	
2698 METHYL CINNAMATE	23	1.9	3.8	8.7	13.	1.7 14.	2.7 40.	*Condiments* (1)0.40
2699 6-METHYLCOUMARIN	10	5.2	4.8	21.	24.	39.	0.80 15.	
2700 METHYLCYCLOPENTENOLONE--3-Methylcyclopentane-1,2-dione; Cyclotene; Kentonarome	22	11.	5.6	18.	13.	(1)14.	8.0 15.	*Syrups* 10. 30.
2701 4-(3,4-METHYLENEDIOXYPHENYL)-2-BUTANONE--Piperonyl acetone	7	8.2	45.	40.	40.			
2702 5-METHYLFURFURAL	2	(1)0.13	(1)0.13	0.03 0.13	(1)0.03			
2703 METHYL 2-FUROATE--Methyl pyromucate	4	0.61	0.06 1.3	0.66	1.0 1.3			*Condiments* (1)0.02
2704 2-METHYL-3-FURYLACROLEIN--α-Methyl furylacrolein	5	0.60	0.65	0.68	0.92			
2705 METHYL HEPTANOATE	5	0.80	0.83	0.33	0.50 0.60			
2706 2-METHYLHEPTANOIC ACID--2-Methyloenanthic acid; Methylamylacetic acid	1	(1)1.0	(1)10.	(1)10.	(1)10.			
2707 6-METHYL-5-HEPTEN-2-ONE	12	1.1	1.1	1.1	1.3	(1)1.3		
2708 METHYL HEXANOATE	4	4.1	8.5	5.3	(1)20.			
2709 METHYL 2-HEXENOATE	2	0.03 0.12		(1)0.03				
2710 METHYL *p*-HYDROXYBENZOATE--Methylparaben; Methyl parasept; Nipagin; Tegosept M	2	(1)5.0	(1)5.0	(1)5.0	5.0 8.0			
2711 METHYL-α-IONONE--5-(2,6,6-Trimethyl-2-cyclohexen-1-yl)-4-penten-3-one; Raldeine®; α-Cetone	14	1.7	2.4	6.6	6.5		(1)0.60	*Jellies* (1)0.21
2712 METHYL-β-IONONE--5-(2,6,6-Trimethyl-1-cyclohexen-1-yl)-4-penten-3-one; Raldeine®; β-Cetone	11	2.0	2.2	7.5	5.9			
2713 METHYL-δ-IONONE--5-(2,6,6-Trimethyl-3-cyclohexen-1-yl)-4-penten-3-one	9	0.61	0.89	3.2	2.8			

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2714 α-*iso*-METHYLIONONE--4-(2,6,6-Trimethyl-2-cyclohexen-1-yl)-3-methyl-3-buten-2-one; Methyl-γ-ionone (so-called)	14	0.97	0.98	4.9	4.3	(1)0.05	(1)0.80			
2715 METHYL LAURATE--Methyl dodecanoate	3	0.50 5.0	0.50 5.0	0.02 0.50	(1)1.0					
2716 METHYL MERCAPTAN--Methanethiol	3	0.56	0.13 1.0	0.13 1.0	0.15 1.0					
2717 METHYL o-METHOXYBENZOATE--o-Methoxy methyl benzoate	1	(1)12.	(1)9.0	(1)30.	(1)40.					
2718 METHYL N-METHYLANTHRANILATE--Dimethyl anthranilate; 2-Methylamino methylbenzoate	22	5.1	5.0	18.	17.		*Jellies* (1)4.0			
2719 METHYL 2-METHYLBUTYRATE	1	(1)5.0	(1)10.	(1)10.	(1)10.					
2720 METHYL 2-METHYLTHIOPROPIONATE--Methyl β-methyl mercaptopropionate; Methyl β-methiopropionate	10	0.35	0.37	0.74	1.0			*Syrups* (1)0.05		
2721 METHYL 4-METHYLVALERATE--Methyl 4-methylpentanoate; Methyl *iso*-caproate; Methyl *iso*-butylacetate	1	(1)11.	(1)44.	(1)33.	(1)33.					
2722 METHYL MYRISTATE--Methyl tetradecanoate	4	0.25 0.50	0.25 0.50	2.4	0.30 2.0	(1)0.24				
2723 METHYL β-NAPHTHYL KETONE--2'-Acetonaphthone; Oranger crystals; Cetone D	12	0.50	0.75	5.3	2.0	2.2 3.0	480. 700.			
2724 METHYL NONANOATE	6	3.9	3.6	6.2	7.1					
2725 METHYL 2-NONENOATE--Neofolione	6	3.2	12.	9.9	13.					
2726 METHYL 2-NONYNOATE--Methyl octyne carbonate	9	0.69	0.28	0.61	2.2	0.02 0.12		*Condiments* (1)10.		
2727 2-METHYLOCTANAL--Methyl hexyl acetaldehyde	2	(1)1.0	(1)1.0	(1)2.0	(1)2.0					
2728 METHYL OCTANOATE	4	0.02 1.0	1.0 10.	13.	1.0 40.					
2729 METHYL 2-OCTYNOATE--Methyl heptine carbonate; Folione®	24	0.15	0.30	1.4	1.4	1.7 1.7	13. 20.	*Jellies* (1)0.23		
2730 4-METHYL-2,3-PENTANEDIONE--Acetyl *iso*-butyryl	13	7.6	5.6	6.2	8.3	1.2 18.				
2731 4-METHYL-2-PENTANONE--Methyl *iso*-butyl ketone	1	(1)6.3	(1)6.3	(1)6.3	(1)6.3					
2732 β-METHYLPHENETHYL ALCOHOL--Hydratropyl alcohol; 2-Phenyl-1-propanol	4	1.1	0.42	1.2	0.92					
2733 METHYL PHENYLACETATE--Methyl α-toluate	21	3.9	2.5	13.	12.	(1)0.10	(1)11.	*Syrups* (1)37.		
2734 3-METHYL-4-PHENYL-3-BUTENE-2-ONE--Benzylidene acetone methyl	5	0.59	2.0	2.8	2.0					
2735 2-METHYL-4-PHENYL-2-BUTYL ACETATE--Dimethyl phenethyl carbinyl acetate	4	1.8	(1)0.50	0.50 10.	0.50 10.					
2736 2-METHYL-4-PHENYL-2-BUTYL *iso*-BUTYRATE--Dimethyl phenethyl carbinyl *iso*-butyrate	3	0.50 11.	1.0 44.	11.	2.0 30.					
2737 2-METHYL-4-PHENYLBUTYRALDEHYDE	1	(1)0.02	(1)0.50	(1)0.50	(1)0.50					
2738 3-METHYL-2-PHENYLBUTYRALDEHYDE--α-*iso*-Propyl phenylacetaldehyde	2	(1)0.10	(1)0.50	0.32 0.50						
2739 METHYL 4-PHENYLBUTYRATE	4	0.56	0.52	1.6	1.4					
2740 4-METHYL-1-PHENYL-2-PENTANONE--Benzyl *iso*-butyl ketone	2	(1)1.0	(1)5.0	0.06 5.0	(1)5.0					

F E M A No. and Substance	No. of Reports	Beverages	Ice Cream, Ices, Etc.	Candy	Baked Goods	Gelatins and Puddings	Chewing Gum	—Other Category Uses—		
2741 THYL 3-PHENYLPROPIONATE--Methyl hydro-cinnamate	4	0.46	0.56	1.7	0.70 4.0					
2742 METHYL PROPIONATE	4	20.	29.	96	130.					
2743 2-METHYL-3-(*p-iso*-PROPYLPHENYL) PROPIONALDEHYDE--α-Methyl-*p-iso*-propyl hydrocinnamaldehyde, Cyclamen aldehyde, Cyclamal; α-Methyl-*p-iso*-propyl phenylpropyl aldehyde, Violet Alpine, oil	10	0.30	0.45	0.99	1.2					
2744 4-METHYLQUINOLINE--Lepidine, p-Methylquinoline	4	0.22	1.4	1.8	1.8					
2745 METHYL SALICYLATE	76	59.	27.	840.	54.		8,400.	*Syrups* (1)200.		
2746 METHYL SULFIDE--Dimethyl sulfide	6	1.1	0.30	1.4	1.6	(1)0.13		*Syrups* (1)0.50		
2747 2-METHYLTHIOPROPIONALDEHYDE--Methional; β-Methiopropionaldehyde, Methylmercaptopropionaldehyde	8	0.35	0.01 1.0	0.01 1.0	0.66			*Condiments* 0.62	*Meats* (1)1.9	
2748 2-METHYL-3-TOLYL PROPIONALDEHYDE (Mixed *o-, m-, p-*)	1	(1)0.05	(1)1.0	(1)1.0	(1)1.0					
2749 2-METHYLUNDECANAL--Methyl nonyl acetaldehyde; 2-Methylhendecanal; Aldehyde C-12 MNA	17	0.31	0.11	0.94	1.3	0.80 2.5	(1)0.20	*Jellies* (1)0.33		
2750 METHYL 9-UNDECENOATE	4	3.7	6.7	22.	22.					
2751 METHYL 2-UNDECYNOATE--Methyl decyne carbonate	3	0.10 5.0	(1)20.	(1)15.	(1)15.					
2752 METHYL VALERATE	4	9.1	25.	28.	39.					
2753 THYL *iso*-VALERATE	6	9.3	26.	26.	30.		(1)35.			
2754 2-METHYLVALERIC ACID--2-Methylpentanoic acid	1	-	-	(1)0.60	-					
2755 MIMOSA, ABSOLUTE--*Acacia decurrens* Willd. var. *dealbata*	8	0.79	21.	1.7	17.					
2756 MONOSODIUM GLUTAMATE	29	-	-	(1)1.3	61.			*Condiments* 1,900. *Soups* 4,300.	*Meats* 2,900.	*Pickles* (1)130.
2757 MOUNTAIN MAPLE, EXTRACT SOLID--*Acer spicatum* Lam.	4	(1)100.	(1)8.0	2.0 60.	44.					
2758 MUSK AMBRETTE--2,6-Dinitro-3-methoxy-1-methyl-4-*tert*-butylbenzene	13	0.43	0.26	4.8	0.41	(1)0.01	(1)9.0			
2759 *MUSK TONQUIN--*Moschus moschiferus* L.	9	0.67	0.62	2.0	2.7			*Syrups* (1)3.0		
2760 *MUSTARD, BROWN [*Brassica juncea* (L.) Coss. (brown); *B. nigra* (L.) Koch (blk.)]--Mustard, black	6	-	-	-	-			*Condiments* 5,200.	*Meats* 2,300.	
2761 *MUSTARD, YELLOW [*Brassica hirta* Moench (*B. alba* (L.) Boiss.)]--Mustard, white	23	(1)350.	-	-	(1)20.			*Condiments* 8,200.	*Meats* 1,400.	*Pickles* 2,500. 38,000.
2762 MYRCENE--7-Methyl-3-methylene-1,6-octadiene.	5	4.4	6.4	0.50 13.	4.9					
2763 MYRISTALDEHYDE--Tetradecanal; Tetradecyl aldehyde, Aldehyde C-14 (Myristic)	5	2.7	0.06 8.0	1.9	0.08 24.	(1)0.15				
2764 MYRISTIC ACID--Tetradecanoic acid	6	5.3	2.6 10.	4.1	5.3	(1)0.10				
2765 MYRRH, GUM--*Commiphora molmol* Engler; *C. abyssinica* (Berg) Engler; and other *Commiphora* spp.	5	84.	- (1)0.13	0.13 10.	(1)0.15		(1)1.2	*Soups* (1)10.		
2766 MYRRH, OIL--*Commiphora molmol* Engler; *C. abyssinica* (Berg) Engler; and other *Commiphora* spp.	4	3.3	8.3	13.	13.					
2767 β-NAPHTHYL ANTHRANILATE--2-Naphthyl anthranilate	9	2.3	1.1	16.	19.					

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FEMA No. and Substance	No. of Reports	Beverages	Ice Cream, Ices, Etc.	Candy	Baked Goods	Gelatins and Puddings	Chewing Gum	— Other Category Uses —		
2768 β-NAPHTHYL ETHYL ETHER--2-Ethoxynaphthalene, Ethyl 2-naphthyl ether; Nerolin; Neroline	14	0.65	0.74	2.8	3.6	(1)0.12				
2769 *NARINGEN, EXTRACT--*Citrus paradisi* Macf.	9	71.	5.7	-	-			*Alcoholic Beverages* (1)0.20		
2770 NEROL--cis-3,7-Dimethyl-2,6-octadien-1-ol; Nerosol	10	1.4	3.9	16.	19.	1.0 1.3	(1)0.80			
2771 *NEROLI BIGARDE, OIL [*Citrus aurantium* L.]--Orange flowers, bitter, oil	36	2.0	3.2	8.9	16.		(1)40.			
2772 NEROLIDOL--3,7,11-Trimethyl-1,6,10-dodecatrien-3-ol; Peruviol	5	0.91	0.92	3.5	2.0 8.0					
2773 NERYL ACETATE	11	1.3	1.6	5.1	15.					
2774 NERYL BUTYRATE	6	6.2	22.	16.	25.					
2775 NERYL *iso*-BUTYRATE	6	1.2	1.8	3.3	5.4					
2776 NERYL FORMATE	6	5.3	23.	17.	22.					
2777 NERYL PROPIONATE	6	6.3	23.	21.	21.					
2778 NERYL *iso*-VALERATE	5	0.97	1.6	4.0	5.7					
2779 *NITROUS OXIDE	1	-	-	-	-					
2780 2,6-NONADIEN-1-OL	2	(1)0.01	(1)0.05	0.05 0.50	(1)0.01			*Alcoholic Beverages* (1)0.01		
2781 γ-NONALACTONE--4-Hydroxynonanoic acid, γ-lactone; γ-Amyl butyrolactone; Aldehyde C-18 (so-called); Prunolide; Coconut Aldehyde	38	11.	14.	33.	55.	28.	(1)15.	*Icings* 25.		
2782 NONANAL--Pelargonic aldehyde; Pelargonaldehyde; Aldehyde C-9	17	1.3	1.3	4.1	2.3	(1)6.0	0.20 38.			
2783 1,3-NONANEDIOL ACETATE (Mixed esters)--Octyl crotonyl acetate; Nonylene glycol diacetate, Jasmonyl; Diasmol	2	0.30 1.0	0.50 1.0	1.5 6.0	1.5 4.0					
2784 NONANOIC ACID--Pelargonic acid; Nonoic acid; Nonylic acid	5	1.8	7.8	6.6	13.			*Shortening* (1)10.		
2785 2-NONANONE--Methyl heptyl ketone	5	0.55	0.10 1.0	0.40 4.0	0.40 4.0					
2786 3-NONANON-1-YL ACETATE--Methylol methyl hexyl ketone acetate; Ketone alcohol ester; Compound 1051	2	(1)0.30	(1)0.30	0.80 5.0	(1)1.0			*Condiments* (1)10.		
2787 NONANOYL 4-HYDROXY-3-METHOXYBENZYL-AMIDE--Pelargonyl vanillylamide; N-(4-Hydroxy-3-methoxybenzyl) nonanamide; N-Nonanoyl vanillylamide	1	-	-	(1)10.	(1)10.			*Condiments* (1)10.		
2788 NONYL ACETATE--Acetate C-9	6	0.81	0.81	1.9	3.1					
2789 NONYL ALCOHOL--1-Nonanol; Alcohol C-9, Nonalol	9	0.70	0.61	2.0	1.9		(1)18.			
2790 NONYL OCTANOATE	2	(1)2.0	-	-	(1)0.06					
2791 NONYL *iso*-VALERATE	3	0.50 1.0	0.50	1.0 2.0	1.4					
2792 *NUTMEG--*Myristica fragrans* Houtt.	44	700.	550.	-	2,000.			*Condiments* (1)100.	*Meats* 670.	*Pickles* (1)100.
2793 *NUTMEG, OIL--*Myristica fragrans* Houtt.	75	14.	13.	19.	75.		1.2 640.	*Condiments* 21. *Syrups* (1)16.	*Icings* 2.0 30.	*Meats* 150.

FEMA No. and Substance	No. of Reports	Beverages	Ice Cream, Ices, Etc.	Candy	Baked Goods	Gelatins and Puddings	Chewing Gum	— Other Category Uses —		
IPS, EXTRACT--*Quercus alba* L.	5	2.5 21.	2.5 84.	2.5 63.	(1)63.			*Alcoholic Beverages* 1,000. 1,000.		
2795 OAK MOSS, ABSOLUTE--*Evernia prunastri* (L.) Ach., *E. furfuracea* (L.) Mann, and other lichens	8	1.8	0.41	0.81	2.5	(1)0.15		*Condiments* (1)40.	*Soups* (1)0.50	
2796 γ-OCTALACTONE--4-Hydroxyoctanoic acid, γ-lactone	9	4.8	16.	16.	17.	(1)15.		*Syrups* (1)57.		
2797 OCTANAL--Caprylaldehyde; Caprylic aldehyde; Octylaldehyde; Aldehyde C-8	18	1.4	1.6	3.4	4.4	3.0 6.1	(1)0.10			
2798 OCTANAL DIMETHYL ACETAL--1,1-Dimethoxyoctane; C-8 Dimethylacetal	4	0.74	0.78	2.8	2.8			*Alcoholic Beverages* (1)3.0		
2799 OCTANOIC ACID--Caprylic acid; Octoic acid; C-8	11	2.9	2.0	13.	18.			*Condiments* (1)12.		
2800 1-OCTANOL--Octyl alcohol; Heptyl carbinol; *pri*-Octyl alcohol; Capryl alcohol; Caprylic alcohol; Alcohol C-8	12	2.9	0.91	2.8	3.0	(1)1.5	16. 57.			
2801 2-OCTANOL--secondary Octyl alcohol, secondary Capryl alcohol; Methyl hexyl carbinol	1	•	(1)0.60	(1)3.0	(1)4.0	(1)2.0				
2802 2-OCTANONE--Methyl hexyl ketone	7	0.10 1.0	0.20 1.0	0.40 4.0	0.40 4.0					
2803 3-OCTANONE--Ethyl amyl ketone; EAK	8	3.3	10.	11.	11.					
2804 3-OCTANON-1-OL--Methylol methyl amyl ketone; Ketone alcohol; Compound 1010	2	(1)0.20	(1)0.30	(1)0.80	0.60 0.80			*Condiments* (1)1.0		
2805 1-OCTEN-3-OL--Amyl vinyl carbinol	1	(1)0.20	(1)1.0	(1)2.0	(1)6.0			*Condiments* (1)6.0	*Soups* (1)6.0	
. ACETATE--2-Ethyl hexyl acetate; Acetate C-8	8	1.6	0.87	4.7	6.0					
2807 OCTYL BUTYRATE	6	0.59	1.3	2.9	2.9					
2808 OCTYL *iso*-BUTYRATE	6	2.0	2.4	3.5	3.5		(1)0.50			
2809 OCTYL FORMATE	4	0.01 1.0	(1)1.0	5.0	7.0					
2810 OCTYL HEPTANOATE	2	0.13 1.0	0.13 1.0	0.13 2.0	0.20 2.0					
2811 OCTYL OCTANOATE	2	0.50 1.0	0.50 1.0	0.50 2.0	0.50 2.0					
2812 OCTYL PHENYLACETATE	4	1.3	(1)1.0	0.20 4.0	(1)4.0					
2813 OCTYL PROPIONATE	5	0.84	0.57	3.6	2.0 4.0					
2814 OCTYL *iso*-VALERATE	4	0.90	0.80 1.0	1.0 4.0	1.0 4.0					
2815 OLEIC ACID--9-Octadecenoic acid; Oleinic acid	10	0.25 0.40	30.	3.5	25.			*Condiments* (1)0.02		
2816 OLIBANUM, OIL [*Boswellia carteri* Birdw. and other *Boswellia* spp.]--Frankincense	4	0.60	1.2	3.3	3.7					
2817 *ONION, OIL--*Allium cepa* L.	20	(1)0.50	(1)0.50	(1)0.50	1.9			*Condiments* 2.2	*Meats* 10.	*Pickles* (1)16.
2818 *ORANGE BLOSSOMS, ABSOLUTE--*Citrus aurantium* L.	3	1.7	7.3	5.7	1.0 15.		(1)10.			
2819 NGE FLOWERS--*Citrus aurantium* L.	2	100. 2,000.	•	•	•					
2820 *ORANGE LEAF, ABSOLUTE--*Citrus aurantium* L.	1	(1)0.02	(1)0.10	(1)0.25	(1)0.25					
2821 *ORANGE, OIL, DISTILLED--*Citrus sinensis* (L.) Osbeck	19	130.	140.	690.	440.	45. 500.	(1)930.			

FEMA No. and Substance	No. of Reports	Beverages	Ice Cream, Ices, Etc.	Candy	Baked Goods	Gelatins and Puddings	Chewing Gum	— Other Category Uses —		
2822 *ORANGE, OIL, TERPENELESS--*Citrus sinensis* (L.) Osbeck	49	10.	17.	38.	25.	230.	13. 160.	*Condiments* (1)25.		
2823 *ORANGE PEEL, BITTER, OIL--*Citrus aurantium* L.	29	67.	71.	150.	110.	(1)300.	(1)500.	*Alcoholic Beverages* (1)4.0		
2824 *ORANGE PEEL, SWEET, EXTRACT--*Citrus sinensis* (L.) Osbeck	10	99.	170.	320. - 330.	320. 330.					
2825 *ORANGE PEEL, SWEET, OIL--*Citrus sinensis* (L.) Osbeck	104	210.	330.	1,000.	430.	1,300.	4,200.	*Alcoholic Beverages* (1)5.0 *Condiments* (1)32.	*Breakfast Cereals* (1)40. *Icings* 190.	*Meats* (1)10. *Syrups* (1)0.34
2826 *ORANGE PEEL, SWEET, OIL, TERPENELESS--*Citrus sinensis* (L.) Osbeck	6	43.	83.	190.	240.	(1)600.				
2827 *OREGANO [Mexican: *Lippia* spp., usually *L. graveolens* HBK European: *Origanum* spp. Elsewhere: Other genera, including *Coleus*, *Lantana*, and *Hyptis*]--Oreganum; Mexican oregano; Mexican sage, Origan	22	(1)320.	.	.	(1)400.			*Condiments* 2,800.	*Meats* 540.	
2828 *ORIGANUM, OIL (EXTRACTIVE) [*Thymus capitatus* Hoffm. et Link (syn. *Coridothymus capitatus* Reichb.)]--Spanish origanum	12	(1)0.50	(1)0.50	(1)0.50	0.60 33.			*Condiments* 30.	*Meats* 37.	
2829 ORRIS, CONCRETE, LIQUID, OIL[b] --*Iris florentina* L.	41	1.7	0.52	1.1	1.3	(1)0.86	8.8	*Icings* (1)4.0		
2830 ORRIS ROOT, EXTRACT[b] [*Iris florentina* L.]--White flag, extract	22	9.2	29.	56.	31.	(1)2.0	10. 120.			
2831 *PALMAROSA, OIL--*Cymbopogon martini* (Roxb.) Stapf	7	4.2	1.7	12.	13.					
2832 PALMITIC ACID--Hexadecanoic acid; Hexadecylic acid; Cetylic acid	1	.	.	.	.			*Condiments* (1)1.0		
2833 *PAPRIKA--*Capsicum annuum* L.	31	.	.	.	1,900.			*Condiments* 970.	*Meats* 7,400	*Soups* 1,000. 7,500.
2834 *PAPRIKA, OLEORESIN--*Capsicum annuum* L.	17	1.0 25.	(1)1.0	0.86	(1)1.2			*Condiments* 100.	*Meats* 96.	
2835 *PARSLEY--*Petroselinum crispum* (Miller) Nyman (*P. sativum* Hoffm.)	18	(1)3,000.	.	.	(1)850.			*Condiments* 2,700.	*Meats* 1,000.	*Soups* 200. 500.
2836 *PARSLEY, OIL--*Petroselinum crispum* (Miller) Nyman (*P. sativum* Hoffm.)	17	1.4	0.20 0.25	4.1	8.5			*Condiments* 4.9		
2837 *PARSLEY, OLEORESIN--*Petroselinum crispum* (Miller) Nyman (*P. sativum* Hoffm.)	2	.	.	.	.			*Condiments* 5.0 30.		
2838 PATCHOULY, OIL--*Pogostemon cablin* Benth. and *P. heyneanus* Benth.	12	0.88	1.1	6.3	10.		43. 220.			
2839 PENNYROYAL, OIL [*Hedeoma pulegioides* (L.) Pers. (American); *Mentha pulegium* L. var. *eriantha* (European and North African)]--Hedeoma, oil	4	1.5 5.0	3.7	14.	20. 24.					
2840 ω-PENTADECALACTONE--15-Hydroxypentadecanoic acid,ω-lactone; Cyclopentadecanolide; 14-Hydroxytetradecanoic acid; Thibetolide®; Angelica lactone; Exaltolide; Pentadecanolide	8	0.27	0.68	1.4	1.8	(1)0.10		*Alcoholic Beverages* (1)0.50		
2841 2,3-PENTANEDIONE--Acetyl propionyl	16	0.60	3.3	5.9	9.6	0.28		*Toppings* (1)0.30		
2842 2-PENTANONE--Methyl propyl ketone; Ethyl acetone	3	13.	34.	32.	32.					
2843 4-PENTENOIC ACID--Allyl acetic acid	1	(1)1.0	(1)2.0	(1)5.0	(1)5.0			*Margarine* (1)2.0		

[b] The expert panel can find no evidence for oral sensitivity to orris root, extract, and orris concrete.

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FEMA No. and Substance	No. of Reports	Beverages	Ice Cream, Ices, Etc.	Candy	Baked Goods	Gelatins and Puddings	Chewing Gum	— Other Category Uses —		
ER, BLACK--*Piper nigrum* L.	33	(1)30.	-	-	1,200.			*Condiments* 690. *Meats* 1,700.	*Pickles* 7.2 230.	*Soups* 27 100.
•PEPPER, BLACK, OIL--*Piper nigrum* L.	15	2.7	0.10 20.	5.3	8.5			*Condiments* 17.	*Meats* (1)140.	
•PEPPER, BLACK, OLEORESIN--*Piper nigrum* L.	21	15.	1.0 20.	1.0 15.	1,600.			*Condiments* 370.	*Meats* 230.	
•PEPPERMINT LEAVES--*Mentha piperita* L.	5	-	-	-	-					
•PEPPERMINT, OIL--*Mentha piperita* L.	81	99.	110.	1,200.	300.	75. 200.	8,300.	*Alcoholic Beverages* 240. *Meats* (1)8.0	*Icings* 5.0 54.	*Toppings* 650.
•PEPPER, RED--*Capsicum frutescens* L. (*C. annuum* L.)	28	15. 240.	-	-	270.			*Condiments* 630.	*Meats* 310.	*Pickles* 11. 59.
•PEPPER, WHITE--*Piper nigrum* L.	22	5.9 140.	-	-	(1)450.			*Condiments* 2,700.	*Meats* 600.	*Soups* (1)500.
•PEPPER, WHITE, OIL--*Piper nigrum* L.	3	-	-	-	(1)0.60					
•PEPPER, WHITE, OLEORESIN--*Piper nigrum* L.	6	-	-	-	-			*Meats* (1)50.		
•PETITGRAIN, LEMON, OIL--*Citrus limon* (L.) Burm. f.	3	8.6	9.3	35.	35.					
•PETITGRAIN, MANDARIN, OIL--*Citrus reticulata* Blanco var. *mandarin*	14	4.3	4.1	4.5	11.	(1)0.43				
•PETITGRAIN, OIL--*Citrus aurantium* L.	27	1.8	1.4	5.3	17.	(1)0.20	4.1	*Condiments* (1)15.		
LANDRENE--*p*-Mentha-1,5-diene; 2-Methyl-iso-propyl-1,3-cyclohexadiene	11	10.	28.	130.	41.					
PHENETHYL ACETATE--2-Phenylethyl acetate; Benzyl carbinyl acetate	17	1.4	2.2	4.2	8.6					
PHENETHYL ALCOHOL--β-Phenylethyl alcohol; 2-Phenylethyl alcohol; Benzyl carbinol	30	1.8	8.3	12.	16.	(1)0.15	21. 80.			
PHENETHYL ANTHRANILATE--2-Phenylethyl anthranilate	9	1.4	1.9	6.2	5.8					
PHENETHYL BENZOATE--2-Phenylethyl benzoate	5	1.0	1.0	2.0	(1)4.0		(1)3.8			
PHENETHYL BUTYRATE--2-Phenylethyl butyrate	10	3.2	8.9	13.	13.					
PHENETHYL *iso*-BUTYRATE--2-Phenylethyl *iso*-butyrate	12	3.4	4.0	13.	11.					
PHENETHYL CINNAMATE--2-Phenylethyl cinnamate	7	1.7	0.80	3.2	3.1	(1)0.10				
PHENETHYL FORMATE--2-Phenylethyl formate	8	1.3	11.	13.	15.					
PHENETHYL 2-FUROATE--2-Phenylethyl 2-furoate	2	(1)0.03	-	(1)0.03	(1)0.03					
PHENETHYL PHENYLACETATE--2-Phenylethyl phenylacetate	13	2.3	4.2	4.8	5.3			*Maraschino Cherries* (1)10.		
PHENETHYL PROPIONATE--2-Phenylethyl propionate	10	3.6	11.	12.	16.					
THYL SALICYLATE--2-Phenylethyl salicylate	5	0.75	0.67	1.5	2.0 2.0					
PHENETHYL SENECIOATE--Phenethyl 3,3-dimethylacrylate; 2-Phenylethyl senecioate; Phenethyl 3-methylcrotonate	1	-	(1)5.0	(1)5.0	-			*Alcoholic Beverages* (1)5.0		

FEMA No. and Substance	No. of Reports	Beverages	Ice Cream, Ices, Etc.	Candy	Baked Goods	Gelatins and Puddings	Chewing Gum	— Other Category Uses —	
2870 PHENETHYL TIGLATE--2-Phenylethyl tiglate	5	0.80 0.90	4.3	10.	10.				
2871 PHENETHYL *iso*-VALERATE--2-Phenylethyl *iso*-valerate; Phenethyl 3-methylbutyrate	13	1.3	2.5	5.9	6.1		0.80 45.		
2872 PHENOXYACETIC ACID--Phenoxyethanoic acid; O-Phenylglycolic acid; Phenylium	4	0.37	1.0	2.2	2.2				
2873 2-PHENOXYETHYL *iso*-BUTYRATE	3	0.90 5.0	5.0 30.	15. 30.	15. 30.				
2874 PHENYLACETALDEHYDE--α-Toluic aldehyde; α-Tolualdehyde; Hyacinthin	8	0.68	0.75	1.6	2.0		1.7 87.		
2875 PHENYLACETALDEHYDE 2,3-BUTYLENE GLYCOL ACETAL	2	-	-	(1)4.0	-				
2876 PHENYLACETALDEHYDE DIMETHYL ACETAL--Viridine	6	0.40	0.78	1.4	8.8		(1)1.0		
2877 PHENYLACETALDEHYDE GLYCERYL ACETAL	2	(1)5.0	(1)20.	0.06 20.	-				
2878 PHENYLACETIC ACID--α-Toluic acid	25	1.8	5.3	5.9	12.	(1)27.	5.4 11.	*Alcoholic Beverages* (1)0.10	*Syrups* (1)0.10
2879 4-PHENYL-2-BUTANOL--Phenylethyl methyl carbinol	3	0.12 0.90	0.60 6.0	1.5 15.	1.5 15.				
2880 4-PHENYL-3-BUTEN-2-OL--Methyl styryl carbinol	2	(1)2.0	(1)20.	0.03 20.	(1)20.				
2881 4-PHENYL-3-BUTEN-2-ONE--Benzilidene acetone; Methyl styryl ketone; Benzylacetone	12	0.82	0.84	3.7	4.5	(1)2.1		*Shortening* (1)0.20	
2882 4-PHENYL-2-BUTYL ACETATE--Phenylethyl methyl carbinyl acetate	3	0.10 3.0	(1)3.0	(1)3.0	0.50 3.0				
2883 1-PHENYL-3-METHYL-3-PENTANOL--Phenylethyl methyl ethyl carbinol	1	(1)0.16	-	(1)0.16	-	(1)0.60			
2884 1-PHENYL-1-PROPANOL--Phenyl ethyl carbinol	1	(1)0.50	(1)0.50	(1)1.5	(1)1.5				
2885 3-PHENYL-1-PROPANOL--Hydrocinnamyl alcohol; Benzylethyl alcohol; Phenylpropyl alcohol	8	0.73	1.4	3.8	3.3		(1)4.3	*Alcoholic Beverages* (1)5.0	
2886 2-PHENYLPROPIONALDEHYDE--Hydratropaldehyde; 2-Phenylpropanal; α-Methyl phenylacetaldehyde; α-Methyl tolualdehyde	5	0.61	0.30	0.85	0.85				
2887 3-PHENYLPROPIONALDEHYDE--Hydrocinnamaldehyde; Phenylpropyl aldehyde; Benzylacetaldehyde	10	1.0	1.7	5.0	5.5	(1)4.3			
2888 2-PHENYLPROPIONALDEHYDE DIMETHYL ACETAL--Hydratropaldehyde dimethyl acetal	11	0.26	0.51	1.5	3.1		(1)5.0	*Condiments* (1)5.0	
2889 3-PHENYLPROPIONIC ACID--Hydrocinnamic acid; Benzylacetic acid	4	0.02 1.0	0.48 1.0	0.80 4.0	17.	(1)1.2		*Dairy Products* (1)2.0	*Toppings* (1)1.0
2890 3-PHENYLPROPYL ACETATE--Hydrocinnamyl acetate	14	3.2	4.8	4.6	6.3		(1)10.	*Condiments* (1)0.10	
2891 2-PHENYLPROPYL BUTYRATE--β-Methylphenethyl butyrate; Hydratropyl butyrate; α-Phenylpropyl alcohol, butyric ester	1	(1)1.0	(1)1.0	(1)2.0	(1)2.0				
2892 2-PHENYLPROPYL *iso*-BUTYRATE--Hydratropyl *iso*-butyrate, α Phenylpropyl alcohol, *iso*-butyric ester	1	(1)5.0	(1)20.	(1)20.	-				
2893 3-PHENYLPROPYL *iso*-BUTYRATE--Hydrocinnamyl *iso*-butyrate	7	1.3	3.0	5.0	5.8				
2894 3-PHENYLPROPYL CINNAMATE--Hydrocinnamyl cinnamate	7	3.4	4.1	4.3	5.3				

FEMA No. and Substance	No. of Reports	Beverages	Ice Cream, Ices, Etc.	Candy	Baked Goods	Gelatins and Puddings	Chewing Gum	— Other Category Uses —		
2895 PHENYLPROPYL FORMATE--Hydrocinnamyl formate	3	1.3	0.90 1.5	3.0 5.0	2.7					
2896 3-PHENYLPROPYL HEXANOATE--Hydrocinnamyl hexanoate	4	0.67	1.3	3.3	3.7					
2897 3-PHENYLPROPYL PROPIONATE--Hydrocinnamyl propionate	4	0.49	0.52	2.0	2.4		0.80 50.			
2898 2-(3-PHENYLPROPYL)-TETRAHYDROFURAN--2-Hydrocinnamyl tetrahydrofuran	2	(1)0.50	(1)2.0	0.03 2.0	-	(1)2.0	(1)2.3			
2899 3-PHENYLPROPYL *iso*-VALERATE--Hydrocinnamyl iso-valerate	4	0.90	0.90	1.8	1.7					
2900 PHOSPHORIC ACID	43	510.	660.	(1)5,000.	(1)1,500.					
2901 *PIMENTA LEAF, OIL--*Pimenta officinalis* Lindl.	25	2.8	1.3	35.	32.	(1)0.06	(1)80.	*Condiments* 80.	*Meats* 160.	
2902 α-PINENE--2-Pinene; 2,6,6-Trimethylbicyclo-(3.1.1)-2-heptene	10	16. 54.	(1)64.	(1)48.	160.			*Condiments* 2.6 150.		
2903 β-PINENE--2(10)-Pinene; Nopinene	3	0.05 16.	(1)64.	48. 600.	48. 600.					
2904 PINE NEEDLE, DWARF, OIL [*Pinus mugo* Turra var. *pumilio* (Haenke) Zenari]--Pinus pumilio, oil, Pine, mountain, oil	5	0.39	0.63	1.9	1.9					
2905 PINE NEEDLE, OIL [*Abies sibirica* Ledeb.; *A. alba* Mill.; *A. sachalinensis* Masters; *A. mayriana* Miyabe and Kudo]--Siberian fir, oil	5	1.5	0.62	5.2	2.7					
2906 PINE, SCOTCH, OIL--*Pinus sylvestris* L.	3	(1)6.0	-	(1)3.0	(1)2.0					
2907 PINE TAR, OIL [*Pinus palustris* Mill. and other spp. of *Pinus*]--Tar, oil	3	-	(1)2.0	(1)10.	-					
2908 PIPERIDINE--Hexahydropyridine	2	(1)3.0	-	(1)5.0	0.05 5.0			*Condiments* (1)0.05	*Meats* (1)0.05	*Soups* (1)0.05
2909 PIPERINE--Piperoylpiperidine	1	(1)0.01	-	-	-					
2910 *d*-PIPERITONE--*p*-Menth-1-en-3-one; 1-Methyl-4-*iso*-propyl-1-cyclohexen-3-one	5	1.0 11.	18.	18.	18.					
2911 PIPERONAL--Heliotropine, Piperonyl aldehyde; Dioxymethylene protocatechuic aldehyde; 3,4-Methylenedioxybenzaldehyde	48	6.0	7.0	7.4	18.	5.8	36.			
2912 PIPERONYL ACETATE--Heliotropyl acetate	2	27. 50.	80. 110.	70. 80.	55. 80.					
2913 PIPERONYL *iso*-BUTYRATE	3	0.05 1.0	(1)0.05	0.05 3.5	0.10 3.5					
2914 *PIPSISSEWA LEAVES, EXTRACT--*Chimaphila umbellata* Nutt.	6	41.	-	(1)75.	-					
2915 POLYSORBATE 20--Polyoxyethylene (20) sorbitan monolaurate, Tween® 20	6	180.	(1)500.	200. 1,000.	200. 1,000.			*Condiments* (1)380.		
2916 POLYSORBATE 60--Polyoxyethylene (20) sorbitan monostearate; Tween® 60	11	110.	150.	280.	1,600.	(1)100.	(1)28.	*Soups* (1)4,000.	*Toppings* 5,000. 12,000.	
2917 POLYSORBATE 80--Polyoxyethylene (20) sorbitan monooleate, Tween® 80	35	170.	200.	300.	320.			*Soups* (1)200.	*Pickles* 100. 120.	*Toppings* (1)8,000.
2918 *POMEGRANATE BARK, EXTRACT--*Punica granatum* L.	0	-	-	-	-					
2919 *POPPY SEED--*Papaver somniferum* L.	10	-	-	-	8,600.					

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FEMA No. and Substance	No. of Reports	Beverages	Ice Cream, Ices, Etc.	Candy	Baked Goods	Gelatins and Puddings	Chewing Gum	— Other Category Uses —		
2920 POTASSIUM ACETATE	1	(1)1.5	.	.	.					
2921 POTASSIUM SORBATE	12	110.	(1)580.	.	100. 1,000.			*Cottage Cheese* (1)500.	*Meats* (1)20.	
2922 PROPENYLGUAETHOL--6-Ethoxy-m-anol; 2-Propenyl-6-ethoxyphenol; 1-Ethoxy-2-hydroxy-4-propenylbenzene; Hydroxymethyl anethole; Vanitrope®	17	5.9	6.3	20.	20.	(1)2.5				
2923 PROPIONALDEHYDE--Propanal; Methylacetaldehyde; Propyl aldehyde	5	3.9	12.	11.	13.					
2924 PROPIONIC ACID--Propanoic acid; Methylacetic acid; Ethylformic acid	6	1.2 5.8	6.0	14.	20.			*Cheese* (1)600.		
2925 PROPYL ACETATE	12	4.0	16.	12.	14.					
2926 iso-PROPYL ACETATE	5	16.	17.	58.	75.					
2927 p-iso-PROPYLACETOPHENONE	2	(1)0.08	(1)0.10	(1)0.50	(1)1.0			*Pickles* (1)5.0		
2928 PROPYL ALCOHOL--1-Propanol; Propylic alcohol; Optal	2	0.50 5.0	(1)0.50	(1)0.50	(1)0.65					
2929 iso-PROPYL ALCOHOL--2-Propanol; iso-Propanol; Petrohol; Dimethylcarbinol	10	(1)25.	.	10. 75.	(1)75.					
2930 p-PROPYL ANISOLE--Dihydroanethole; Propyl methoxybenzene	4	4.3	9.9	64.	67.					
2931 PROPYL BENZOATE	1	(1)11.	(1)44.	(1)33.	(1)33.					
2932 iso-PROPYL BENZOATE	1	(1)0.50	(1)1.0	(1)1.0	(1)1.0					
2933 p-iso-PROPYLBENZYL ALCOHOL--p-Cymen-7-ol; Cuminic alcohol; Cumin alcohol; Cuminyl alcohol; Cuminol	5	11.	0.47	33.	35.					
2934 PROPYL BUTYRATE	8	6.8	4.6	24.	16.					
2935 iso-PROPYL BUTYRATE	5	9.7	21.	39.	39.					
2936 PROPYL iso-BUTYRATE	8	6.8	4.8	24.	20.					
2937 iso-PROPYL iso-BUTYRATE	3	12. 25.	18. 25.	58. 100.	60. 100.					
2938 PROPYL CINNAMATE	7	2.6	2.9	4.9	4.3	(1)0.07				
2939 iso-PROPYL CINNAMATE	5	0.52	0.75	1.3	2.3					
2940 PROPYLENE GLYCOL--1,2-Propanediol; Methyl glycol; 1,2-Dihydroxypropane	89	690.	810.	1,300.	1,300.	250. 290.	1,800.	*Maraschino Cherries* (1)300. *Pickles* (1)20. *Syrups* (1)7,000.	*Icings* (1)0.08 *Soups* (1)20.	*Meats* 10. 40. *Toppings* 3,800.
2941 PROPYLENE GLYCOL ALGINATE	6	(1)200.	800. 2,100.	.	.			*Condiments* 1,000. 50,000.	*Icings* (1)150.	
2942 PROPYLENE GLYCOL STEARATE--Propylene glycol octadecanoate	2	.	.	17. 5,000.	43. 20,000.			*Toppings* (1)100,000.		
2943 PROPYL FORMATE	5	20.	57.	65.	85.					
2944 iso-PROPYL FORMATE	2	18. 25.	18. 25.	55. 100.	60. 100.					
2945 PROPYL 2-FURANACRYLATE--Propyl 3-(2-furyl) acrylate	2	(1)3.0	.	(1)0.03	.					

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FEMA No. and Substance	No. of Reports	Beverages	Ice Cream, Ices, Etc.	Candy	Baked Goods	Gelatins and Puddings	Chewing Gum	— Other Category Uses —		
2946 ?OPYL 2-FUROATE	2	-	-	(1)0.03	(1)0.03			Condiments (1)0.20		
2947 PROPYL GALLATE--Tenox P G[3]	9	0.08	0.05	0.16	0.97	(1)0.03				
2948 PROPYL HEPTANOATE	4	3.8	5.1	5.9	18.			Alcoholic Beverages (1)3.0		
2949 PROPYL HEXANOATE	5	2.2	3.0	8.0	-					
2950 iso-PROPYL HEXANOATE	2	(1)0.50	5.5 10.	20. 40.	20. 40.					
2951 PROPYL p-HYDROXYBENZOATE--Propylparaben; Propylparasept; Nipasol	2	0.20 32.	(1)130.	(1)96.	(1)96.					
2952 3-PROPYLIDENEPHTHALIDE	1	-	(1)5.0	(1)5.0	(1)5.0					
2953 α-PROPYLPHENETHYL ALCOHOL--1-Phenyl-2-pentanol; Benzylpropyl carbinol; Benzylbutyl alcohol	1	(1)1.0	(1)5.0	(1)5.0	-	(1)5.0				
2954 p-iso-PROPYLPHENYLACETALDEHYDE--p-Cymen-7-carboxaldehyde	1	(1)0.10	(1)0.50	(1)0.50	-					
2955 PROPYL PHENYLACETATE	4	0.30 1.0	0.30 1.5	2.7	1.0 5.0					
2956 iso-PROPYL PHENYLACETATE	3	0.20 0.50	1.8	0.50 8.0	3.0 4.0					
2957 3-(p-iso-PROPYL)PHENYL PROPIONALDEHYDE--p-iso-Propyl hydrocinnamaldehyde; Cuminyl acetaldehyde	3	(1)0.80	(1)0.80	(1)1.3	(1)3.0		(1)5.0			
2958 PROPYL PROPIONATE	9	6.0	12.	25.	25.					
2959 iso-PROPYL PROPIONATE	3	9.7	5.0 50.	40. 50.	30. 50.					
2960 PROPYL iso-VALERATE	7	5.0	16.	17.	20.					
2961 iso-PROPYL iso-VALERATE	5	3.4	3.4	11.	11.					
2962 iso-PULEGOL--p-Menth-8-en-3-ol	4	7.4	29.	23.	23.					
2963 PULEGONE--p-Menth-4(8)-en-3-one; Δ-4(8)-p-Menthen-3-one; 1-Methyl-4-iso-propylidene-3-cyclohexanone	3	5.0 8.0	5.0 32.	17.	24. 25.					
2964 iso-PULEGONE--p-Menth-8-en-3-one, Δ-8(9)-p-Menthen-3-one; 1-Methyl-4-iso-propenyl-3-cyclohexanone	3	4.0	12.	16.	16.					
2965 iso-PULEGYL ACETATE	4	5.8	22.	19.	19.					
2966 PYRIDINE	3	(1)1.0	0.02 0.12	(1)0.40	(1)0 40					
2967 PYROLIGNEOUS ACID*	16	10.	15.	51.	33.	(1)30.		Meats 30. 300.		
2968 PYROLIGNEOUS ACID, EXTRACT*	4	-	-	-	50. 200.			Alcoholic Beverages (1)20.	Meats 100. 300.	
2969 PYRUVALDEHYDE--Pyruvic aldehyde; Acetylformaldehyde; 2-Ketopropionaldehyde; 2-Oxopropanal	2	(1)1.0	(1)1.0	0.03 5.0	0.03 5.0					
2970 PYRUVIC ACID--Pyroracemic acid, Acetylformic acid, 2-Ketopropionic acid, 2-Oxopropanoic acid, α-Ketopropionic acid	5	(1)0.25	0.25 20.	27.	30.		(1)110.			
2971 QUASSIA, EXTRACT [*Picrasma excelsa* (Sw.) Planch., *Quassia amara* L.]--Bitter wood, extract, Bitter ash, extract	12	3.4	-	-	(1)50.			Alcoholic Beverages 3.4		

* Prior Sanction - *Federal Register*, November 30, 1957, Page 9594, Section 3.201

FEMA No. and Substance	No. of Reports	Beverages	Ice Cream, Ices, Etc.	Candy	Baked Goods	Gelatins and Puddings	Chewing Gum	— Other Category Uses —		
2972 QUEBRACHO BARK, EXTRACT--*Aspidosperma quebracho-blanco* Schlecht., or *Schinopsis lorentzii* (Griseb.) Engl.	4	11.	23.	27.	28.					
2973 QUILLAIA [*Quillaja saponaria* Molina]--Soap bark; Saponin; China bark, extract	22	95.	(1)0.12	(1)18.	-			*Syrups* (1)6.8		
2974 *QUINCE SEED, EXTRACT--*Cydonia oblonga* Mill. (*C. vulgaris* Pers.)	3	0.01 40.	0.06 20.	-	(1)1.0					
2975 QUININE BISULFATE	2	95. 100.	-	-	-					
2976 QUININE HYDROCHLORIDE	19	110.	-	-	-					
2977 QUININE SULFATE	6	100.	-	-	-					
2978 *iso*-QUINOLINE	3	(1)0.25	(1)0.25	(1)1.0	0.004 1.0					
2979 RHATANY, EXTRACT [*Krameria triandra* Ruiz et Pavon (Peruvian); *K. argentea* Martius (Brazilian)]--Krameria, extract	7	11.	31.	40.	8.0 63.			*Alcoholic Beverages* (1)10.		
2980 RHODINOL--3,7-Dimethyl-7-octen-1-ol; (Commercial Rhodinol is largely *l*-Citronellol)	28	2.0	2.1	7.6	8.1	(1)2.9	(1)31.	*Jellies* (1)0.92		
2981 RHODINYL ACETATE	10	2.8	1.4	9.4	18.					
2982 RHODINYL BUTYRATE	7	0.94	1.1	3.0	8.7		(1)1.1			
2983 RHODINYL *iso*-BUTYRATE	9	1.1	1.8	3.3	4.5	(1)0.01				
2984 RHODINYL FORMATE	9	1.3	1.8	4.3	4.9	(1)0.08				
2985 RHODINYL PHENYLACETATE	7	1.2	1.2	3.8	4.4					
2986 RHODINYL PROPIONATE	7	1.8	2.4	4.9	5.8					
2987 RHODINYL *iso*-VALERATE	5	2.0	2.3	7.2	7.2					
2988 *ROSE, ABSOLUTE--*Rosa alba* L.; *R. centifolia* L. and varieties of these spp.	11	0.63	1.2	2.0	1.6					
2989 *ROSE, BULGARIAN, TRUE OTTO, OIL [*Rosa damascena* Mill.]--Attar of roses	24	0.51	0.68	2.6	1.2	0.01 0.50	15.	*Jellies* (1)0.05		
2990 *ROSE HIPS, EXTRACT [*Rosa canina* L.; *R. gallica* L.; *R. condita* Scop.; *R. rugosa* Thunb.; and other *Rosa* spp.]--Hipberries, extract	1	-	-	-	-					
2991 *ROSEMARY--*Rosmarinus officinalis* L.	15	(1)700.	-	-	-			*Condiments* 680.	*Meats* 380.	
2992 *ROSEMARY, OIL [*Rosmarinus officinalis* L.]--Garden rosemary, oil	17	3.6	0.50 4.0	7.5	6.3			*Condiments* 2.9	*Meats* (1)40.	
2993 *ROSE WATER, STRONGER--*Rosa centifolia* L.	2	(1)100.	-	-	-					
2994 *RUE--*Ruta graveolens* L.	2	-	-	-	(1)6.0					
2995 *RUE, OIL--*Ruta graveolens* L.	13	1.2	1.3	4.1	3.3			*Condiments* (1)1.0		
2996 RUM ETHER†--Ethyl oxyhydrate	53	67.	110.	320.	230.	(1)1.7	380.	*Alcoholic Beverages* 80. 1,600.		
2997 SACCHARINE, SODIUM SALT--1,2-Benzisothiazolin-3-one, 1,1-dioxide, sodium salt; Kristallose; Crystallose; Saccharin soluble	8	72.	(1)150.	2,100. 2,600.	(1)12.					

† Rum ether shall consist of at least 99 per cent water, ethyl alcohol, ethyl acetate, methanol, ethyl formate, acetone, acetaldehyde, and formaldehyde. It shall all distill at a temperature not exceeding 100°C. at atmospheric pressure, and shall leave no residue on evaporation. The methanol and formaldehyde contents, combined, shall not exceed 5 per cent.

FEMA No. and Substance	No. of Reports	Beverages	Ice Cream, Ices, Etc.	Candy	Baked Goods	Gelatins and Puddings	Chewing Gum	— Other Category Uses —		
2998 SAFFRON--*Crocus sativus* L.	11	(1)1.3	•	•	(1)10.			*Alcoholic Beverages* (1)200.	*Meats* 260.	
2999 *SAFFRON, EXTRACT [*Crocus sativus* L.]--Crocus, extract	5	1.3 7.5	1.3 9.0	6.3	1.9 14.			*Condiments* (1)50.		
3000 *SAGE--*Salvia officinalis* L.	25	(1)300.	•	•	170.			*Meats* 1,800.		
3001 *SAGE, OIL--*Salvia officinalis* L.	22	3.7	16.	11.	14.		(1)30.	*Condiments* 14.	*Meats* 110.	*Pickles* (1)2.4
3002 *SAGE, OLEORESIN--*Salvia officinalis* L.	7	•	•	•	•			*Condiments* (1)100.	*Meats* 100.	
3003 *SAGE, SPANISH, OIL --*Salvia lavandulaefolia* Vahl.	8	2.0 11.	2.0 44.	20.	20.			*Condiments* (1)50.	*Meats* 40. 40.	
3004 SALICYLALDEHYDE--*o*-Hydroxybenzaldehyde	10	0.55	1.1	1.8	6.3		11. 18.	*Alcoholic Beverages* (1)5.0	*Condiments* (1)2.0	
3005 SANDALWOOD, YELLOW, OIL [*Santalum album* L.]--Sandalwood, East Indian, oil; Saunders, white, oil; Arheol	8	2.4	7.5	7.7	6.6		(1)47.			
3006 SANTALOL (α-and β-)--Arheol	2	0.06 2.0	0.35 2.0	1.0 10.	1.0 8.0		(1)0.20			
3007 SANTALYL ACETATE	4	0.53	0.78	2.0	2.0		(1)2.3			
3008 SANTALYL PHENYLACETATE	3	1.0	0.95	2.0	2.0					
3009 SARSAPARILLA, EXTRACT [b]--*Smilax* spp.	9	190.	130.	(1)1,000.	(1)2,000.					
3010 SASSAFRAS BARK, EXTRACT (Safrol-free)--*Sassafras albidum* (Nutt.) Nees	5	290.	(1)10.	(1)100.	(1)50.					
3011 SASSAFRAS LEAVES (Safrol-free)--*Sassafras albidum* (Nutt.) Nees	2	•	•	•	•			*Soups* (1)30,000.		
3012 *SAVORY, SUMMER--*Satureja hortensis* L.	8	•	•	•	800. 850.			*Condiments* (1)200.	*Meats* 1,100.	
3013 *SAVORY, SUMMER, OIL--*Satureja hortensis* L.	2	•	•	(1)4.0	(1)4.0			*Condiments* 10. 50.		
3014 *SAVORY, SUMMER, OLEORESIN--*Satureja hortensis* L.	2	•	•	(1)4.0	(1)4.0			*Condiments* 35. 50.		
3015 *SAVORY, WINTER--*Satureja montana* L.	0	•	•	•	•					
3016 *SAVORY, WINTER, OIL--*Satureja montana* L.	1	•	•	(1)4.0	(1)4.0			*Condiments* (1)50.		
3017 *SAVORY, WINTER, OLEORESIN--*Satureja montana* L.	1	•	•	(1)4.0	(1)4.0			*Condiments* (1)80.		
3018 *SCHINUS MOLLE, OIL [*Schinus molle* L.]--Pepper tree, oil	4	•	•	(1)10.	(1)10.			*Condiments* (1)3.0		
3019 SKATOLE--3-Methylindole; β-Methylindole	8	0.75	1.0	0.78	0.80	(1)0.01	(1)0.10			
3020 *SLOE BERRIES [*Prunus spinosa* L.]--Blackthorn berries	2	•	•	•	•					
3021 *SLOE BERRIES, EXTRACT [*Prunus spinosa* L.]--Blackthorn berries, extract	7	110.	50. 100.	(1)40.	(1)45.			*Alcoholic Beverages* 43,000.		
3022 *SLOE BERRIES, EXTRACT SOLID [*Prunus spinosa* L.]--Blackthorn berries, extract solid	0	•	•	•	•					
3023 SNAKEROOT, CANADIAN, OIL [*Asarum canadense* L.]--Wild ginger, Canadian, oil	9	1.9	1.0 5.0	8.3	8.3			*Condiments* 1.4 4.0		
3024 SODIUM ACETATE	4	(1)1.5	(1)15.	(1)200.	(1)15.			*Breakfast Cereals* (1)60.		

[b] Judged solely on the basis of common use.

FEMA No. and Substance	No. of Reports	Beverages	Ice Cream, Ices, Etc.	Candy	Baked Goods	Gelatins and Puddings	Chewing Gum	— Other Category Uses —		
3025 SODIUM BENZOATE	89	350.	39.	350.	300.		(1)12.			
3026 SODIUM CITRATE--(Trisodium citrate); Citratin; Citrosodine	47	490.	(1)15.	(1)40.	220.			*Meats* 40. 600.	*Toppings* 50. 3,900.	
3027 SODIUM HEXAMETAPHOSPHATE--Sodium metaphosphates, Calgon; Giltex; Quadrafos; Micromet; Hagen phosphate	6	-	-	-	-	500. 7,000.		*Breakfast Cereals* (1)3,000.		
3028 SORBITAN MONOSTEARATE--Span® 60	6	140.	(1)5.0	9.0 7,300.	1,400.			*Cheese* (1)8.0	*Condiments* (1)8.0	
3029 *d*-SORBITOL--*d*-Glucitol, Sorbit, Sorbol, Sorbo; Nevitin; Karion; Sionon; Diakarmon	24	1,300.	70,000.	21,000.	50,000.	(1)8,000.		*Icings* (1)500.	*Toppings* (1)280,000.	
3030 *SPEARMINT--*Mentha spicata* L.	5	(1)500.	-	-	-.			*Condiments* (1)1,000.	*Meats* (1)500.	
3031 *SPEARMINT, EXTRACT--*Mentha spicata* L.	4	2,100.	(1)100.	(1)0.20	-					
3032 *SPEARMINT, OIL--*Mentha spicata* L.	47	100.	81.	830.	270.	(1)75.	6,200.	*Alcoholic Beverages* (1)100.	*Jellies* 72. 1,900.	
3033 *SPIKE LAVENDER, OIL--*Lavandula latifolia* Vill. (*L. spica* DC.)	5	10. 11.	10. 44.	18.	33. 50.					
3034 SPRUCE, OIL [*Tsuga canadensis* (L.) Carr.; *T. heterophylla* (Raf.) Sarg.; *Picea mariana* (Mill.); *P. glauca* (Moench) Voss]--Hemlock, oil	15	6.2	15.	11.	2.0 4.0	(1)1.0	(1)44.			
3035 STEARIC ACID--Octadecanoic acid	4	2.0 10.	-	(1)4,000.	(1)3.5					
3036 STORAX [*Liquidambar orientalis* Mill.; *L. styraciflua* L.]--Styrax, gum	8	2.0	2.0	13.	23.		(1)300.	*Toppings* (1)15.		
3037 STYRAX, EXTRACT--*Liquidambar orientalis* Mill.; *L. styraciflua* L.	5	0.84	0.25 0.60	3.5	4.8 6.0	(1)0.04				
3038 SUCROSE OCTAACETATE	2	0.35 20.	-	-	-					
3039 SULFUR DIOXIDE--Sulfurous anhydride; Sulfurous oxide	10	180.	(1)2.5	-	-			*Condiments* (1)400.	*Dehydrated Potatoes* (1)60.	*Soups* (1)20.
3040 TAGETES, OIL [*Tagetes erecta* L.; *T. patula* L.; or *T. glandulifera* Schrank]--Marigold, oil	8	4.1	7.4	9.0	13.	(1)7.0		*Condiments* (1)20.		
3041 *TANGERINE, OIL--*Citrus reticulata* Blanco	43	90.	160.	160.	280.	(1)20.	810.			
3042 TANNIC ACID [Nut galls of *Quercus infectoria* Oliv. and related spp. of *Quercus*]--Gallotannic acid; Tannin	5	1.1 45.	(1)160.	0.20 100.	40.			*Alcoholic Beverages* 6.0 1,000.		
3043 *TARRAGON--*Artemisia dracunculus* L.	16	-	-	-	(1)20.			*Condiments* 23.	*Meats* 260.	
3044 TARTARIC ACID (*d*-, *l*-, *dl*-, *meso*-)--Racemic acid	45	960.	570.	5,400.	1,300.	(1)60.	(1)3,700.	*Condiments* (1)10,000.		
3045 α-TERPINEOL--*p*-Menth-1-en-8-ol	24	5.4	16.	14.	19.	12. 16.	40.	*Condiments* (1)38.		
3046 TERPINOLENE--*p*-Menth-1,4(8)-diene; 1,4(8)-Terpadiene	2	(1)16.	(1)64.	0.12 48.	(1)49.					
3047 TERPINYL ACETATE--*p*-Menth-1-en-8-yl acetate	19	3.8	3.2	9.9	15.		14. 260.	*Condiments* (1)15.	*Meats* 1.7 40.	
3048 TERPINYL ANTHRANILATE--*p*-Menth-1-en-8-yl anthranilate	3	1.1	1.5 2.6	6.3	6.0 6.0					
3049 TERPINYL BUTYRATE--*p*-Menth-1-en-8-yl butyrate	4	6.4	9.2	11.	9.5		(1)210.			
3050 TERPINYL *iso*-BUTYRATE--*p*-Menth-1-en-8-yl *iso*-butyrate	2	0.90 2.4	(1)5.0	4.0 15.	5.0 15.					

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FEMA No. and Substance	No. of Reports	Beverages	Ice Cream, Ices, Etc.	Candy	Baked Goods	Gelatins and Puddings	Chewing Gum	— Other Category Uses —		
3051 RPINYL CINNAMATE--*p*-Menth-1-en-8-yl cinnamate	1	(1)0.50	(1)2.6	(1)6.0	(1)6.0			*Alcoholic Beverages* (1)1.0		
3052 TERPINYL FORMATE--*p*-Menth-1-en-8-yl *formate*	3	0.50 3.0	2.6 5.0	6.0 10.	6.0 10.					
3053 TERPINYL PROPIONATE--*p*-Menth-1-en-8-yl propionate	3	1.5	2.6 3.0	6.0 10.	6.0 10.					
3054 TERPINYL *iso*-VALERATE--*p*-Menth-1-en-8-yl *iso*-valerate	2	0.50 5.0	2.6 5.0	6.0 10.	6.0 10.					
3055 TETRAHYDROFURFURYL ACETATE	3	1.3 2.0	(1)8.0	1.0 20.	1.0 20.					
3056 TETRAHYDROFURFURYL ALCOHOL--Tetrahydro-2-furanmethanol; Tetrahydro-2-furylmethanol; Tetrahydro-2-furancarbinol; THFA	2	0.03 14.	(1)0.03	0.03 18.	(1)0.04					
3057 TETRAHYDROFURFURYL BUTYRATE	1	(1)0.90	(1)6.0	(1)15.	(1)15.					
3058 TETRAHYDROFURFURYL PROPIONATE	3	1.3 2.0	(1)8.0	1.0 20.	1.0 20.					
3059 TETRAHYDRO-*pseudo*-IONONE--6,10-Dimethyl-9-undecen-2-one	4	0.50 0.50	0.60 2.4	14.	14.					
3060 TETRAHYDROLINALOÖL--3,7-Dimethyloctan-3-ol	5	1.3	2.7	5.6	5.6					
3061 TETRAMETHYL ETHYLCYCLOHEXENONE (Mixture of isomers)	1	(1)5.0	(1)30.	(1)30.	(1)30.					
3062 2-THIENYL MERCAPTAN--2-Thienylthiol	1	-	-	(1)0.10	(1)0.10					
3063 *THYME--*Thymus vulgaris* L.	24	(1)13.	-	(1)5.0	550.			*Meats* 360.	*Soups* 500. 1,000.	
3064 THYME, OIL--*Thymus vulgaris* L.	14	1.0 5.0	(1)20.	1.0 15.	1.5 5.3		(1)100.	*Condiments* 18.	*Meats* 33.	*Soups* (1)0.13
3065 *THYME, WHITE, OIL--*Thymus vulgaris* L.	9	0.01 1.0	(1)0.01	27.	5.4			*Alcoholic Beverages* (1)5.0	*Condiments* 4.0 8.0	*Meats* 15.
3066 THYMOL--3-*p*-Cymenol; 5-Methyl-2-*iso*-propylphenol; Thyme camphor	10	2.5 11.	(1)44.	9.4	5.0 6.5		(1)100.			
3067 TOLUALDEHYDE GLYCERYL ACETAL (Mixed *o*-, *m*-, *p*-)	3	0.08 6.0	6.0 8.0	12. 15.	12. 15.					
3068 TOLUALDEHYDES (Mixed *o*-, *m*-, *p*-)	27	11.	16.	25.	28.	8.3	430.	*Maraschino Cherries* (1)100.		
3069 TOLU, BALSAM, EXTRACT--*Myroxylon balsamum* L. Harms (*M. toluiferum* HBK.)	8	32.	150.	57.	71.		2.0 38.			
3070 TOLU, BALSAM, GUM--*Myroxylon balsamum* L. Harms (*M. toluiferum* HBK.)	7	2.6	13.	5.2	8.0			*Syrups* (1)3.0		
3071 *p*-TOLYLACETALDEHYDE--*p*-Methylphenylacetaldehyde	2	-	(1)2.0	0.03 2.0	(1)2.0					
3072 *o*-TOLYL ACETATE--*o*-Cresyl acetate; Acetyl *o*-cresol; *o*-Cresylic acetate	5	2.8	2.6	11.	9.0 10.	(1)1.0	0.30 220.			
3073 *p*-TOLYL ACETATE--*p*-Cresyl acetate; Acetyl *p*-cresol; *p*-Cresylic acetate	6	0.50 1.0	1.3	4.3	4.4		0.30 220.	*Condiments* (1)10.		
3074 4-(*p*-TOLYL)-2-BUTANONE--*p*-Methylbenzyl acetone	2	(1)1.0	(1)1.5	(1)6.0	(1)6.0					
3075 *p*-TOLYL *iso*-BUTYRATE--*p*-Cresyl *iso*-butyrate	2	0.10 4.0	(1)0.05	0.12 6.0	0.12 7.0					
3076 *p*-TOLYL LAURATE--*p*-Tolyl dodecanoate; *p*-Cresyl dodecanoate; *p*-Cresyl laurate	1	(1)1.0	(1)1.0	(1)2.0	(1)2.0					
3077 *p*-TOLYL PHENYLACETATE--*p*-Cresyl phenylacetate	9	1.6	0.87	4.8	5.4					

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FEMA No. and Substance	No. of Reports	Beverages	Ice Cream, Ices, Etc.	Candy	Baked Goods	Gelatins and Puddings	Chewing Gum	— Other Category Uses —		
3078 2-(*p*-TOLYL)-PROPIONALDEHYDE--*p*-Methylhydratropaldehyde	2	(1)0.13	(1)0.13	(1)0.13	(1)0.20			*Alcoholic Beverages* (1)0.005		
3079 *TRAGACANTH, GUM--*Astragalus gummifer* Lab. or other Asiatic spp. of *Astragalus*	70	42.	65.	67.	140.	(1)2,000.	(1)170.	*Condiments* 470.	*Meats* 50. 60.	
3080 TRIBUTYL ACETYLCITRATE--Citroflex A-4	1	(1)0.40	-	-	-					
3081 TRICALCIUM PHOSPHATE	25	1,000.	46.	50. 60.	80.	700.		*Condiments* (1)540.	*Meats* 360.	
3082 2-TRIDECENAL	2	0.10 0.30	1.6 6.0	4.0 6.0	4.0 6.0		(1)0.10			
3083 TRIETHYL CITRATE--Ethyl citrate	13	13.	47.	180.	230.	(1)10.				
3084 *TUBEROSE, OIL--*Polianthes tuberosa* L.	5	0.26	0.45	1.5	1.7					
3085 *TURMERIC--*Curcuma longa* L.	22	-	-	-	-	(1)0.05		*Condiments* 760. *Soups* 30. 50.	*Meats* 200.	*Pickles* 690.
3086 *TURMERIC, EXTRACT--*Curcuma longa* L.	13	(1)0.78	-	-	-			*Condiments* 89. *Soups* 30. 40.	*Meats* 43. *Pickles* (1)40.	
3087 *TURMERIC, OLEORESIN--*Curcuma longa* L.	13	-	-	-	-			*Condiments* 640.	*Meats* 30. 100.	*Pickles* 200.
3088 TURPENTINE, GUM--*Pinus palustris* Mill. and other *Pinus* spp.	5	-	-	-	(1)15.					
3089 TURPENTINE, STEAM DISTILLED--*Pinus palustris* Mill. and other *Pinus* spp.	6	-	-	11.	10. 20.		(1)7.1			
3090 2,3-UNDECADIONE--Acetyl nonyryl; Acetyl pelargonyl	1	(1)1.5	(1)3.0	(1)3.0	(1)3.0					
3091 γ-UNDECALACTONE--4-Hydroxyundecanoic acid, γ-lactone; γ-Undecyl lactone; γ-Heptyl butyrolactone; Aldehyde C-14 pure (so-called); Peach aldehyde	46	4.4	3.0	11.	7.1	7.5	90.			
3092 UNDECANAL--Undecylic aldehyde; Aldehyde C-11 Undecylic; Hendecanal	6	0.95	3.1	2.0	2.4		(1)56.			
3093 2-UNDECANONE--Methyl nonyl ketone	13	2.8	0.54	2.6	3.1	(1)5.0				
3094 9-UNDECENAL--Undecylenic aldehyde; Hendecen-9-al; Aldehyde C-11 Undecylenic	9	4.8	4.2	4.5	4.6					
3095 10-UNDECENAL	2	0.05 1.0	(1)0.20	(1)0.20	-					
3096 10-UNDECEN-1-yl ACETATE--10-Hendecenyl acetate; Undecenyl acetate; Undecylenic acetate; Acetate C-11	3	3.7	15.	12.	12.					
3097 UNDECYL ALCOHOL--1-Undecanol; Alcohol C-11 Undecylic	4	2.9	15.	12.	12.					
3098 VALERALDEHYDE--Pentanal; Valeric aldehyde; Valeral; Amyl aldehyde	5	1.3	5.0	4.2	5.4					
3099 VALERIAN ROOT, EXTRACT--*Valeriana officinalis* L.	22	25.	35.	65.	69.			*Condiments* (1)24.		
3100 VALERIAN ROOT, OIL--*Valeriana officinalis* L.	18	0.52	0.36	2.6	3.1	0.02 1.5				
3101 VALERIC ACID--Pentanoic acid; Propylacetic acid	16	1.2	1.8	2.5	8.0					

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FEMA No. and Substance	No. of Reports	Beverages	Ice Cream, Ices, Etc.	Candy	Baked Goods	Gelatins and Puddings	Chewing Gum	— Other Category Uses —		
3102 -VALERIC ACID--β-Methylbutyric acid; active Valeric acid; Valerianic acid; *iso*-Propylacetic acid, Delphinic acid; *iso*-Butyl formic acid	19	1.2	14.	12.	5.5			*Cheese* (1)2.4		
3103 γ-VALEROLACTONE--4-Hydroxypentanoic acid, γ-lactone; 3-Methylbutyrolactone; 3-Valerolactone	1	(1)4.0	(1)20.	(1)50.	(1)50.					
3104 *VANILLA--*Vanilla planifolia* Andrews or *V. tahitensis* J. W. Moore	40	420.	600.	490.	530.	630.		*Icings* 200. 630.	*Syrups* (1)10.	*Toppings* (1)300.
3105 *VANILLA, EXTRACT--*Vanilla planifolia* Andrews or *V. tahitensis* J. W. Moore	68	200.	3,000.	4,000.	1,900.			*Icings* 2,000. 4,800.	*Syrups* 8.5 54.	*Toppings* 2,700.
3106 *VANILLA, OLEORESIN--*Vanilla planifolia* Andrews or *V. tahitensis* J. W. Moore	26	190.	290.	210.	300.	(1)230.		*Condiments* (1)200.		
3107 VANILLIN--Methylprotocatechuic aldehyde; Vanillic aldehyde; 4-Hydroxy-3-methoxybenzaldehyde	127	63.	95.	200.	230.	120.	270.	*Chocolate* 970. *Toppings* 150.	*Margarine* (1)0.20	*Syrups* 330. 20,000.
3108 VANILLIN ACETATE--Acetyl vanillin	3	11.	11.	28.	28.					
3109 VERATRALDEHYDE--Vanillin methyl ether; Veratric aldehyde; 3,4-Dimethoxybenzenecarbonal; Dimethyl ether protocatechualdehyde	12	9.0	9.2	32.	30.	(1)15.				
3110 *VIOLET LEAVES, ABSOLUTE--*Viola odorata* L.	5	2.3	8.4	7.6	2.0 24.					
3111 WALNUT HULL, EXTRACT--*Juglans nigra* L. or *J. regia* L.	3	43. 90.	100. 170.	(1)130.	100. 130.					
3112 WINTERGREEN, EXTRACT [*Gaultheria procumbens* L.]--Checkerberry, extract	4	10. 10.	•	900. 5,000.	•					
3113 WINTERGREEN, OIL [*Gaultheria procumbens* L.]--Checkerberry, oil	22	56.	44.	260.	1,300.		3,900.			
3114 WORMWOOD[1] [*Artemisia absinthium* L.]--Absinthium	4	360.	•	•	•			*Alcoholic Beverages* (1)8.0		
3115 WORMWOOD, EXTRACT[1] [*Artemisia absinthium* L.]--Absinthium, extract	8	15. 43.	(1)170.	(1)130.	•			*Alcoholic Beverages* 10. 40.		
3116 WORMWOOD, OIL[1] [*Artemisia absinthium* L.]--Absinthium, oil	11	14.	0.80 32.	9.0	(1)2.0			*Alcoholic Beverages* 11.		
3117 YARROW, HERB [*Achillea millefolium* L.]--Milfoil	6	29.	•	•	•			*Alcoholic Beverages* 6.0 40.		
3118 YERBA SANTA, FLUID EXTRACT--*Eriodictyon californicum* (Hook. and Arn.) Torr.	2	(1)25.	(1)200.	(1)400.	(1)400.					
3119 *YLANG YLANG, OIL--*Cananga odorata* Hook. f. and Thomson	16	0.95	1.4	2.9	2.9		18. 25.	*Icings* (1)0.75		
3120 YUCCA, JOSHUA TREE--*Yucca brevifolia* Engelm.	9	120.	(1)20.	•	•					
3121 YUCCA, MOHAVE, EXTRACT [*Yucca schidigera* Roezl ex Ortgies (*Y. mohavensis* Sarg.)]--Cactus root, extract; Plantarome	10	150.	•	•	•					
3122 *ZEDOARY--*Curcuma zedoaria* (Berg.) Rosc.	4	7.5 2,000.	•	•	•					
3123 *ZEDOARY BARK, EXTRACT--*Curcuma zedoaria* (Berg.) Rosc.	0	•	•	•	•					
3124 ZINGERONE--4-(4-Hydroxy-3-methoxyphenyl)-2-butanone; Zingiberone	6	6.9	7.8	11.	11.		(1)15.			

[1] Provided it is used at levels such that no thujone is detectable in the finished food, using the standard AOAC method.

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National Cancer Institute
Smoking and Health Program

Report No. 3

Toward Less Hazardous Cigarettes

The Third Set of Experimental Cigarettes

Exhibit
R. & Assoc.

U.S. DEPARTMENT OF HEALTH, EDUCATION AND WELFARE
PUBLIC HEALTH SERVICE
NATIONAL INSTITUTES OF HEALTH
DHEW PUBLICATION NO. (NIH) 77-1280

National Cancer Institute
Smoking and Health Program

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Toward Less Hazardous Cigarettes

The Third Set of Experimental Cigarettes

Gio B. Gori, Editor

U.S. DEPARTMENT OF HEALTH, EDUCATION AND WELFARE
Public Health Service
National Institutes of Health
DHEW Publication No. (NIH) 77-1280

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For sale by the Superintendent of Documents, U.S. Government Printing Office
Washington, D.C. 20402
Stock Number 017—043—00127—7

Contents

Foreword

Since the 1964 Surgeon General's Report on the hazards of smoking,[1] the National Clearinghouse for Smoking and Health, the American Cancer Society, and other public health oriented organizations have expanded their efforts to reduce the degree of cigarette smoking nationwide. Political, economic, and cultural factors, however, have prevented widespread effective action in the reduction or elimination of the smoking habit. Today, between 50 and 60 million Americans smoke cigarettes.

The National Cancer Institute, in coordination with the National Heart, Lung and Blood Institute and the Department of Agriculture, has established the Smoking and Health Program to provide guidelines for the reduction of the risks of cigarette smoking. The program is advised by the Tobacco Working Group, a body of consultants representing a wide spectrum of disciplines.

In cooperation since 1968, the Tobacco Working Group and the National Cancer Institute have evolved a systematic approach toward the development of less hazardous cigarettes, presently the most important work of the Smoking and Health Program. The first phase of this approach involves the design of experimental cigarettes and the chemical and biological analyses of their condensate and smoke. Reports on the first and second sets of experimental cigarettes and related chemical and biological analyses were published in March 1974 and January 1975, respectively. This report describes experimentation on the third cigarette series. A fourth experiment began in March 1975 and is currently in progress.

The initial objective of these cigarette experiments is to determine the tumorigenic activity of cigarette smoke condensate when equal weights of dry smoke condensate (as contrasted to equal numbers of cigarettes or equal numbers of puffs) are applied to mouse skin. The components of the tobaccos, the cigarette smoke condensates and whole smokes, and the physical characteristics of the cigarettes provide an extensive amount of laboratory data. These data are correlated with the mouse bioassay data and are analyzed for insights into which smoke components cause adverse health effects. The analyses include an evaluation of the relative hazards of the experimental cigarettes and serve as the basis for the design of more advanced cigarette experiments.

The ultimate objective of these experiments is the design of less hazardous cigarettes for human consumption. Success is hindered by the uncertain relationship between tumors resulting from mouse skin painted with condensate and human lung cancer and by the virtual absence of information on the cardiovascular and respiratory effects of these cigarettes (beyond the permissible inferences from their chemical characteristics). Therefore, the skin painting assays are viewed as screening experiments. It is assumed that reduction of mouse dermal carcinogenic response from smoke condensate is a valid indicator of lines of investigation that are worth pursuing through more sophisticated (and more costly) tests, such as direct inhalation of whole smoke in suitable animal models. Thus the experiments are considered initial steps in the progressive process of improving cigarette characteristics.

The large amount of data (especially chemical) that have shown no significance in the various correlation procedures may be surprising. This reflects, however, the lack of a systematic body of information against which the meaning of these data could be matched in a more constructive way. The publication of this information serves two purposes. First, it may provide the initial nucleus for a taxonomy of analytical data on tobacco and tobacco smoke of specific characteristics, to be amplified by future experiments. Second, it may stimulate others to search for more subtle correlations that may have escaped this initial analysis.

This report begins with a summary of the first and second cigarette experiments. Following a summary of and introduction to the third set of experimental cigarettes are an in-depth description of materials and methods (Section 1), presentation of results (Section 2), and general discussion (Section 3). Specific contributions prepared by Smoking and Health Program participants comprise the remainder of this report and include papers describing and summarizing the tobacco analysis, chemical analysis, cigarette condensate preparation, mouse dorsal skin painting procedures, and cigarette manufacture, as well as supplementary statistical analyses of biological response to the skin painting experiments.

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Director, Smoking and Health Program

[1] Smoking and Health Report of the Advisory Committee to the Surgeon General of the Public Health Service, U.S. Department of Health, Education and Welfare, Washington, D.C., 1964.

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Acknowledgments

Members of The Tobacco Working Group have utilized their scientific and technical expertise to provide guidance for this study. The group was formed in 1968 under the chairmanship of Dr. Carl G. Baker, who was succeeded in 1970 by Dr. Gio B. Gori. Dr. Fred G. Bock assumed the chairmanship in 1975 and Dr. Henry C. McGill in 1976. A list of past and present members follows:

Carl G. Baker	1968-70
William W. Bates	1972-75
Fred G. Bock	1968-
Roswell K. Boutwell	1968-73
Hans L. Falk	1968-70
Alfred Fishman	1973-
Jean D. Gibbons	1974-75
Gio B. Gori	1969-
Michael R. Guerin	1972-74, 1976-
Ian Higgins	1974
Dietrich Hoffmann	1973-75
I. W. Hughes	1972-74, 1976-
Charles J. Kensler	1968-76
Paul Kotin	1968-69
Henry C. McGill, Jr.	1973-
Gardner C. McMillan	1969-
Ian A. Mitchell	1968-70
Thomas B. Owen	1972-
Alan Rodgman	1976-
Umberto Saffiotti	1968-74
Marvin A. Schneiderman	1968-74
Robert B. Seligman	1976-
Irving J. Selikoff	1972-74
Murray Senkus	1968-76
Philippe Shubik	1974-75
A. W. Spears	1968-
Jesse L. Steinfeld	1968-69
T. C. Tso	1968-
Benjamin L. Van Duuren	1968-74
Helmut Wakeham	1968-76
Ernst L. Wynder	1968-73

Many individuals and institutions have cooperated in this experiment, the principal contributors being:

Dr. Gio B. Gori and Dr. Thomas B. Owen (National Cancer Institute)—overall program direction and management

The Tobacco Working Group (National Cancer Institute)—scientific and technical advice

Liggett & Myers Incorporated—cigarette manufacturers

North Carolina State University;
University of Kentucky;
University of Tennessee Tobacco Experimental Station at Greenville;
University of Georgia Tobacco Experimental Station at Tifton;
Peter J. Schweitzer Division, Kimberly-Clark Corporation;
AMF Incorporated;
Philip Morris, U.S.A.;
R. J. Reynolds Tobacco Company;
FMC Corporation;
Imperial Chemical Industries;
Celanese Corporation
—special tobacco processing and supplies

Dr. T. C. Tso, Agricultural Research Service, U.S. Department of Agriculture, in collaboration with University of Kentucky, North Carolina State University, Lorillard Research Center, and other industrial laboratories—tobacco analysis

Dr. A. R. Patel, Maloy Laboratories, Inc.—condensate preparation

Dr. M. R. Guerin, Oak Ridge National Laboratory—smoke and condensate analysis

Mr. J. W. Gargus, Hazleton Laboratories—mouse skin painting

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The National Cancer Institute, Department of Health, Education and Welfare provided overall funding for this project.

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Summary

Experiments conducted since the early fifties have indicated that certain modifications of cigarettes can influence the chemical composition and tumorigenic activity of the resulting smoke and condensate. Some of these findings were sufficiently consistent to enable the prediction of the type of influence exerted by these cigarette modifications. During 1968 and 1969, the Tobacco Working Group and the National Cancer Institute staff reviewed these experiments, consulted with domestic and foreign experts, and formulated a set of experimental cigarette models for subsequent study in the search for the characteristics of a less hazardous cigarette.

Series I. The first cigarette experiment was begun in 1970 with these experimental cigarette models. Two standard cigarette types were adopted as bases of comparison. One was the 1R1 cigarette, developed by the University of Kentucky in the early 1960's and adopted in many studies as a point of comparison. The other was a Standard Experimental Blend (SEB I), designed to represent the tobacco composition of the average American cigarette marketed in 1970.

Twenty-one modifications to SEB I were selected as the experimental variables. These modifications included the use of reconstituted tobacco sheet made from SEB I and variations in paper porosity, in the widths of tobacco cut, in the fraction of SEB I used (such as leaves only and stems only), and in the concentration of nitrate. None of the cigarettes in these experiments was filtered.

Several significant results were obtained from the first experiment. Cigarettes made with high-porosity paper, those made of tobacco stems only, and those made with reconstituted sheets all resulted in condensates less tumorigenic than SEB I on mouse skin. Neither the width of tobacco cuts nor the addition of nitrates to SEB I appeared to affect the condensate tumorigenicity, but cigarettes made of tobacco laminae only were so toxic that the skin painting with their condensate had to be discontinued.

Series II. The second cigarette experiment was begun in 1972, based on results from the first experiment and on agronomic factors.

The University of Kentucky 1R1 and SEB I were again used as reference cigarettes. SEB II, having the same blend as SEB I but produced from a different crop year and made by a different manufacturer, was also used as a standard for comparison. Experimental variables in the second experiment consisted of: variations in tobacco processing, which affect the packing density, the amount of tobacco per cigarette (thus the amount of tar and nicotine), and the aeration of the burning zone (thus the oxygenation and temperature of the burning process); the use of tobacco from plants with normal and low nicotine content to compare relative nicotine toxicity; variations in the concentration of fertilizer (nitrogen) to determine whether high or normal fertilization produces tobaccos whose smoke condensates lead to different tumorigenicity; variations in tobacco leaf processing to determine whether fatty alcohol-treated plants produce leaves causing greater tumorigenic activity than hand-suckered plants; and the use of nontobacco cigarettes to determine the tumorigenicity of alternative artificial smoking materials relative to SEB I, SEB II, and 1R1.

The low nicotine/normal fertilizer and low nicotine/high fertilizer blends showed significantly lower tumorigenicity than the normal nicotine/normal fertilizer blends. There were no significant differences, however, between the low nicotine/normal fertilizer and low nicotine/high fertilizer blends.

The Reynolds puffed, Philip Morris expanded, and freeze-dried SEB II blends showed no significant differences among themselves, but the Philip Morris expanded and freeze-dried SEB II blends showed significantly lower condensate tumorigenicity than SEB II.

One of the two artificial tobacco substitutes (ATS) had the lowest condensate tumorigenicity of all blends tested; the other ATS had the highest. Blends of these materials combined 50/50 with SEB II, however, were not significantly different from SEB II itself. Condensates from the ATS materials were not as homogeneous as tobacco condensates and appeared to differ in physical properties. Further testing of the ATS materials is being done as part of the ongoing fourth cigarette experiment.

The fatty alcohol, fatty alcohol × 100, and hand-suckered blends showed no significant differences among themselves or from the SEB II blend.

The results of the correlation analyses of several constituents of the tobacco, leaf, and condensates of the second cigarette experiment complement those of the first experiment. The concentrations of both nicotine and tar, as constituents of the condensate, were highly correlated with the incidence of tumorigenic activity on mouse skin painted with the condensate. Static burn rate was negatively correlated with tumorigenic activity. Since static burn rate can affect the chemical composition of the smoke, this indicates that a fast burning rate may be a factor in developing less hazardous cigarettes. Other compounds that were negatively correlated with tumorigenicity in both experiments were acetaldehyde, formaldehyde, NO_x, CO, and acrolein. Total phenolics in the leaf, H_2O per cigarette, and benz[a]anthracene in the condensate were positively correlated with tumorigenicity.

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Report on the Third Set of Experimental Cigarettes

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Summary

The third cigarette experiment was begun in 1974, based on results from the first two series, on agronomic factors, and on additional industrial considerations.

The University of Kentucky 1R1 and SEB I were again used as reference cigarettes. SEB III, having the same blend as SEB I but produced from a different crop year and made by a different manufacturer, was also used as a standard for comparison. Experimental variables in the third experiment consisted of:

- tobacco additives that affect the flavor and chemistry of the smoke;
- tobacco additive variations (sugar, cocoa, humectant) that affect the burn rate of the cigarette, the flavor of the smoke, and the tumorigenicity of the condensate;
- variations in paper porosity to evaluate the relationship between this factor and the tumorigenicity of the condensate;
- filter variations to test the effects of filtration on the tumorigenicity of the smoke; and,
- variations in artificial tobacco substitutes (ATS) and physical characteristics to compare their relative tumorigenicity.

The results can be summarized as follows:

- Comparisons among the additive variables indicate that magnesium nitrate reduces the tumorigenicity of cigarette condensate.
- When the additives sugar, humectant, and cocoa are compared, neither sugar nor humectant seems to affect the tumorigenicity of the tobacco smoke at lower (12.5-mg) dose levels but may contribute to tumorigenicity at higher dose levels. Powdered cocoa appears to increase the tumorigenicity of the smoke at both dose levels.
- The dilution filter proved to be effective in reducing the tumorigenicity of the cigarette condensate on an equivalent weight basis. Neither the permanganate filter nor the cellulose acetate filter reduced the tumorigenicity of the condensate.
- There were no significant differences among the paper porosity variables, or between these variables and SEB III.
- Of the two artificial tobacco substitutes (denoted by ATS-A and ATS-B) included in this experiment, the ATS-A cigarette fared well with respect to reducing cigarette tumorigenicity, whereas the ATS-B cigarette fared poorly. Experimental difficulties arose with ATS-B regarding the solvent used in the second and third experiments. This cigarette is being retested during the fourth experiment with a different solvent.

Introduction

This report details the experimental conditions and presents the results obtained, in order to qualify and support the overall conclusion.

The principal sections are Materials and Methods, Results, and Discussion. Experimental details contributed by participating organizations appear in the appendices, and although somewhat lengthy, this additional information aids in understanding the experimental parameters involved in the study.

1. Materials and Methods

This section summarizes the materials and methods used in the third cigarette experiment. The cigarettes were distributed under a randomly selected blind code to the laboratories conducting the bioassays and analyses.

1.1 *The Cigarettes.* During this study, 23 experimental and 2 standard reference types of cigarettes were tested. Table 1 lists the 25 cigarette types and assigns them the variable numbers that are used throughout this report. Six variations of the artificial tobacco substitutes were also tested.

All cigarettes met the following specifications:

Filter: none, unless otherwise specified
Length: 85 mm; ring printed at 23 mm
Circumference: 25 mm
Pressure drop: 8 ± 1 cm of water at a flow rate of 17.5 ml/sec
Weight: ± 1.5% of the mean for each type
Cut: 32 per inch
Paper: 30 cm/min Ecusta Ref. 556

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TABLE 1

Third Series Experimental Cigarettes

Variable No.	Description	Rationale
1	University of Kentucky Reference (1R1)	To provide comparison with Series I and II
2	SEB I	To provide comparison with Series I and II
3	SEB I (3 mg, 6 mg)	
4	SEB III	To provide replicates of SEB III, to estimate variance of the experimental procedure and to provide a base for comparison of the experimental variables
5	SEB III (3 mg, 6 mg)	
6	SEB III	
7	SEB III	
8	SEB III	
9	SEB III with low-porosity paper (5 cm/min)	To evaluate further the effect of paper porosity and to test a special paper. The Coresta method was used to measure paper porosity.
10	SEB III with high-porosity paper (60 cm/min)	
11	SEB III with very high porosity paper (100 cm/min)	
12	SEB III with no sugar	To test the role, if any, of sugars, humectants, and flavorings (cocoa) on tumorigenicity
13	SEB III with no humectant	
14	SEB III with powdered cocoa	
15	SEB III with no sugar, no humectant	
16	SEB III with L&M additive #1	To test the L&M additives
17	SEB III with L&M additive #2	
18	SEB III with L&M additive #3	
19	SEB III burley blend with sugar	To provide further tests of the burley blend and the effect of sugar
20	SEB III burley blend with sugar (3 mg, 6 mg)	
21	SEB III burley blend with no sugar	
22	SEB III with dilution filter	To test dilution filters with and without very high-porosity paper and to test the permanganate filter, for which the acetate filter is a control
23	SEB III with dilution filter and 100 cm/min paper	
24	SEB III with cellulose acetate filter	
25	SEB III with permanganate filter	
26	ATS-A & SEB III 30/70 with flavor	To provide further tests of the ATS-A processed smoking material, with and without high-porosity paper and dilution filter. These may be used later in inhalation bioassays.
27	ATS-A & SEB III 30/70 with 60 cm/min. paper, dilution filter and flavor	
28	ATS-B 100% (old material, old dyes)	To provide further tests of ATS-B processed smoking materials, both as previously tested in Series II and as materials and dyes have been modified by the manufacturer
29	ATS-B 100% (new material, no dyes)	
30	ATS-B 100% (old material, no dyes)	
31	ATS-B (old material, no dyes) & SEB III 50/50	

Packaging: 3750 cig. in each cardboard "filter tray," sealed in polyethylene bags and stored at −20°C

SEB I, II, and III have identical compositions and differ only in manufacturer and crop year. The blend was (by weight):

Glycerol	2.80%
Invert sugar	5.30%
Flue-cured	22.54%
Burley	30.04%
Maryland	1.06%
Turkish	11.09%
Reconstituted sheet[1]	27.17%
	100.00%

[1] Stems and fines in a slurry process. (See Table 6, p. 98.)

Formulas for L&M additives are as follows:

L&M additive #1 magnesium nitrate $Mg(NO_3)_2$	5.72%
L&M additive #2 zinc oxide (ZnO)	7.00%
L&M additive #3 magnesium nitrate	5.61%
zinc oxide	6.90%

1.2 *Tobacco Analyses.* Leaf analyses were conducted at several laboratories, coordinated by Dr. T. C. Tso at the Tobacco Laboratory, Beltsville Agricultural Research Center, Agricultural Research Service, U. S. Department of Agriculture. There were 104 analyses of each sample for individual or grouped components. Full details are given in the tabels on pages 34–48.

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The analyses include:

General and Inorganic
Sand
Crude ash
Alkalinity (pH)
Moisture
Chlorine (Cl)
Sodium (Na)
Potassium (K)
Calcium (Ca)
Magnesium (Mg)
Manganese (Mn)

Carbohydrates and Organic Acids
Starch
Sugar
Cellulose
Chlorogenic acid
Oxalic acid
Malic acid
Citric acid

Nitrogenous Compounds
Total alkaloids
Total volatile bases (TVB)
Nicotine
α-Amino-nitrogen
Ammonia nitrogen (NH_3-N)
Nitrate nitrogen (NO_3-N)
Ammonia (NH_3)
Total nitrogen (N)
Total amino acids
Individual free amino acids

Phenolic Compounds
Total phenolic compounds
Rutin

Fatty Acids, Sterols, Lipids, and Related Compounds
Fatty acids
Phytosterols
Waxes
Glycerol
Petroleum ether extract (nonvolatile)
Lipids residue
Oven volatiles

1.3 *Condensate Preparation.* The cigarettes were removed from freezer storage and conditioned at 25°±1°C and 60% ±5% relative humidity for not less than 48 hr prior to smoking.

The condensates were prepared at Meloy Laboratories (see pages 67–87 for details). The cigarettes were smoked on machines built by Process and Instruments Corporation, with the following specifications:

Operation:	Direct smoking (negative pressure)
Capacity:	Approximately 2000 cigarettes per hr
Puffs:	1/min, 35 ml, 2-sec duration; no more than 10 puffs per cigarette; ejected earlier if smoked to butt
Ambient Air Conditions:	Room air 25° ± 1°C, 60% ± 5% relative humidity; exhaust designed to avoid adverse influences of drafts

Condensate collection. The condensate was collected in four traps at −80°C; the first two traps used 4-mm Pyrex beads, and the second two used Teflon filament.

Extraction. The extraction was with freshly distilled acetone. The condensate was concentrated under reduced pressure at 40°C until less than 8% water remained. Weighed acetone and water were added, the water and nicotine contents were analyzed by gas chromatography, and the mixture was finally adjusted to 500 mg of dry condensate per ml.

Experimental difficulties with phase separation of glycerol/water/tar/acetone systems for the ATS-B condensate were encountered in the second and third experiments. Low-tar cigarettes such as ATS-B have a high relative concentration of glycerol in the condensate and phase separation is observed.

Since analytical laboratory data provided by the ATS-B manufacturer indicated a preferential enrichment of polycyclic aromatic hydrocarbons in the top layer of the ATS-B condensate system in acetone/water, the issue of dosimetry errors was raised.

The possibility of applying the top layer of nonhomogeneous ATS-B condensate in water/acetone systems, although real, was expected to randomize over the long period of the test. It was also suggested that the mixing technique and the brief time that the mixed system stands prior to application argue against any significant skewing of the applied dose due to partitioning of tumorigenic species and inadvertent phase selection. Additionally, it was thought that the use of only the lower portion of round-bottom flasks reduced the probability of nonrandom sampling prior to skin painting.

The phase separation issue was resolved by testing ATS-B condensate in a solvent that would tolerate high glycerol concentrations. This is being done in the fourth cigarette experiment by

using an acetone/water/2-propanol solvent and by following a protocol suggested by the ATS-B supplier. Thus the possibility of a tumorigen phase enrichment/nonrandomization dosimetry error for ATS-B condensate is eliminated in the fourth experiment. Inferences regarding the tumorigenicity of ATS-B condensate should be postponed until results from the fourth experiment are available.

Storage. The condensate was stored at −20°C until sent to the using laboratories and was packed in dry ice for transfer to users.

Production cycle. Condensate preparation schedules were arranged so that all condensate samples were less than 2 months old when used for mouse skin painting.

Quality control. As a quality control, cigarette samples from each batch were used to determine: average weight and pressure drop; static burn rate in draft-free air; combustion zone temperature at 2 butt lengths; and amount of potassium (K), sodium (Na), magnesium (Mg), ash, hexane solubles, nitrate, phosphorus (P), nicotine, total reducing sugar, neophytadiene, and citric, malic, and oxalic acids; and the pH for the smoke condensate.

A monitoring process was carried out measuring: mean butt length after smoking, total dry condensate yield and dry condensate yield per cigarette, pH of the condensate, and percent nicotine in the condensate and per cigarette.

1.4 ***Smoke and Condensate Analyses.*** The smoke and smoke condensate from the various cigarettes were tested at Oak Ridge National Laboratory (see pages 49–66). During the course of the skin painting experiment, condensate was sent to Oak Ridge National Laboratory three times at approximately 6-month intervals. Each shipment was analyzed once within that 6-month period, with quadruplicate determinations per analysis. Analyses were made on whole smoke, gas phase, and particulate matter. The following analyses were conducted:

Cigarette Characteristics
Weight
Resistance to draw

Cigarette Smoke, Condensate, or Both
Colorimetric phenol
Phenol
o-Cresol
m- + p-Cresol
Weak acids
Very weak acids
Total particulate matter
Tar
Water
Nicotine
Nicotine-alkaloids
Palmitic acid
Oleic, linoleic, and linolenic acid
Stearic acid
Neophytadiene

Acetaldehyde
Acrolein
Formaldehyde
Hydrogen cyanide
Oxides of nitrogen
Carbon monoxide
Carbon dioxide
pH
Isoprene
Indole
Skatole
Phenanthrene
Benz[a]anthracene
Benzo[a]pyrene
Total free fatty acids

Smoke analyses were expressed in five ways: per cigarette, per puff, per liter of smoke, per gram of tobacco, and relative to total particulate matter. Condensate components were recorded on a weight-to-weight basis.

In addition to the above determinations, several special analyses were performed on selected condensate batches and on the whole smoke. These include glycerol, catechol, trace metals, metals, and selected sulfur and nitrogen compounds.

1.5 ***Skin Painting Bioassays.*** The skin painting bioassay was conducted at Hazleton Laboratories (see pages 81–87). In line with the first experiment, each condensate was tested at two dose levels on groups of 100 mice each, the daily application being 0.10 ml of a condensate solution containing 12.5 mg or 25 mg of dry smoke condensate. There were 11 exceptions, noted in Table 2.

Three controls were used: mice with dorsal hair clipped but no skin painting; mice painted with acetone only to test the effect of vehicle without condensate; and mice painted with benzo[a]pyrene in acetone at three dose levels, to test the response to a known carcinogen.

Mice. ICR Swiss female mice were randomized five to a cage; cage occupancy was maintained

(see below) but cage positions were changed weekly. The experimental group numbers are shown in Table 2.

Painting. Dorsal hair was clipped weekly. Dose was applied daily (Monday through Saturday); it was measured by syringe and spread uniformly by glass rod. Condensate was throughly shaken (by machine) prior to application. Painting was continued for the duration of the experiment (18 months).

Observations. Routine observations of the mice were made daily by laboratory technicians. If a suspected tumor was observed on any animal for 3 consecutive weeks, it was recorded as a "visually observed tumor." Data entered once a month into computer storage included (where applicable): date of first visually observed tumor, type of tumor (wart-like or gross carcinoma), number of tumors, weight of the animal, and date of death.

Necropsy. All mice dying during the experi-

TABLE 2

Variable/Code/Group Number Identification

Variable No.	Code No.	Group No.	Description*
1	40	35,36	University of Kentucky Reference (1R1)
2	41A	47,48	SEB I
3	41B	25,26	SEB I (3 mg, 6 mg)
4	75A	51,52	SEB III
5	75B	17,18	SEB III (3 mg, 6 mg)
6	72	7,8	SEB III
7	73	53,54	SEB III
8	74	29,30	SEB III
9	76	23,24	SEB III with low-porosity paper (5 cm/min)
10	77	19,20	SEB III with high-porosity paper (60 cm/min)
11	78	37,38	SEB III with very high porosity paper (100 cm/min)
12	80	33,34	SEB III with no sugar
13	81	9,10	SEB III with no humectant
14	82	5,6	SEB III with powdered cocoa
15	83	41,42	SEB III with no sugar, no humectant
16	84	57,58	SEB III with L&M additive #1
17	85	13,14	SEB III with L&M additive #2
18	86	55,56	SEB III with L&M additive #3
19	87A	31,32	SEB III burley blend with sugar (12.5 mg, 12.5 mg)
20	87B	15,16	SEB III burley blend with sugar (3 mg, 6 mg)
21	88	3,4	SEB III burley blend with no sugar (12.5 mg, 12.5 mg)
22	89	61,62	SEB III with dilution filter
23	90	59,60	SEB III with dilution filter and 100 cm/min paper
24	91	43,44	SEB III with cellulose acetate filter
25	92	21,22	SEB III with permanganate filter
26	95	27,28	ATS-A & SEB III 30/70 with flavor (25 mg, 50 mg)
27	96	45,46	ATS-A & SEB III 30/70 with 60 cm/min paper, dilution filter and flavor (25 mg, 50 mg)
28	97	1,2	ATS-B 100% (old material, old dyes) (25 mg, 50 mg)
29	98	49,50	ATS-B 100% (new material, old dyes) (25 mg, 50 mg)
30	0	11,12	ATS-B 100% (old material, no dyes) (25 mg, 50 mg)
31	01	39,40	ATS-B (old material, no dyes) & SEB III 50/50 (25 mg, 50 mg)
Veh. control		63	Acetone
Veh. control		64	Acetone
Neg. control		65	Hair clipped only
Neg. control		66	Hair clipped only
BaP		67	Benzo[a]pyrene (1.25 μg)
BaP		68	Benzo[a]pyrene (2.50 μg)
BaP		69	Benzo[a]pyrene (4.00 μg)

*Except where noted, low dose = 12.5 mg and high dose = 25 mg.

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ments, sacrificed if moribund, or sacrificed on termination of the experiment at 18 months were necropsied and their tissues were fixed in formalin. The target tissue of those mice visually observed to have tumors or suspected of having tumors at necropsy was histopathologically examined. The statistical analysis presented in this report is based on histopathologically verified tumors.

Tumors and nontumorous deaths among experimental animals. In the third cigarette experiment, skin painting was conducted at five condensate dose levels: 3, 6, 12.5, 25, and 50 mg. Three groups of animals were painted with 3 mg of condensate daily, 3 groups with 6 mg, 21 groups with 12.5 mg, 23 groups with 25 mg, and 6 groups with 50 mg. Because of excessive toxicity, both dose groups for variables 19 and 21 were painted at the 12.5-mg condensate dose level. For the purposes of statistical analysis, the SEB III groups were combined, providing 400 animals for this group at the 12.5-mg dose level and another 400 animals for this group at the 25-mg dose level. Animals lost during the first month were replaced. The death rates among untreated controls and negative controls (those receiving acetone only) were approximately 38%. There were no deaths resulting from tumors in any of the untreated or negative controls. The positive controls (those treated with benzo(a)pyrene) had death rates of nearly 100%, with about 76% having tumors at death or necropsy.

Survival probabilities. Actuarial methods[1] were used to estimate the probability (P_t) that an animal within a given group would not develop a tumor if the animal were to survive the 18 months of the experiment. Adjustments were made for those animals that died during the experiment without developing a tumor. (See pages 107–152.) In addition, estimates were calculated of the latent periods (number of days since the initiation of the experiment) to 75%, 50%, and 25% survival (T_{75}, T_{50}, T_{25}).

1.6 ***Bioassays for Ciliatoxic and Cytotoxic Potency.*** The biological potency of the whole smoke from the Series III cigarettes was tested by means of *in vitro* ciliatoxicity and cytotoxicity bioassays. The ciliatoxicity bioassay was performed to determine the extent of ciliary transport inhibition caused by repeated exposure of chicken tracheal epithelium to cigarette smoke. Since ciliary transport is important for maintaining airway patency, the relative ciliatoxicity of the smoke provides a measure of its ability to reduce ciliary clearance. The potency of the smoke was expressed as ED_{50} (the number of 35-ml puffs required to reduce particle transport rates to 50% of the control rate).

The cytotoxicity bioassay was performed to determine the ability of the various smokes to inhibit the growth of mammalian cells grown in vitro. The known cytotoxic effect that cigarette smoke exerts on mammalian cells may influence the maintenance of intact and healthy respiratory tissue. KB tumor cell cultures were utilized.

These bioassays are described on pages 103–106.

2. Results

This section summarizes some of the chemical and physical data derived from the third cigarette experiment.

2.1 ***Cigarette Characteristics.*** Average cigarette weight, resistance to draw, and peak temperatures for each cigarette type are listed on pages 67–80. These characteristics ranged as follows.

Average cigarette weight. Average cigarette weight varied from 937 mg for the SEB III cased burley (variables 19 and 20) to 1307 mg for both the SEB III with L&M additive #3 (variable 18) and the SEB III with a permanganate filter (variable 25).

Resistance to draw. Resistance to draw varied from 24 mm of H_2O per cigarette for the ATS-B (old materials, old dyes; variable 28) to 170 mm of H_2O per cigarette for the SEB III with a permanganate filter (variable 25).

Peak temperatures. The peak temperatures, measured at the 15-mm mark with thermocouple wires, ranged from a low average of 708.1°C for ATS-B (old materials, no dyes) and SEB III 50/50 (variable 31) to a high average of 865.3°C for SEB III with a cellulose acetate filter (variable 24).

2.2 ***Tobacco Analyses.*** The U.S Department of Agriculture made 104 chemical analyses of tobacco leaf for each cigarette variable (see pages 27–48). Table 3 summarizes the lowest and high-

[1] P. Armitage, *Statistical Methods in Medical Research*, Chapter 14, John Wiley and Sons, New York, 1971.

TABLE 3

High and Low Values of Selected Tobacco Leaf Constituents for Cigarettes Composed of at Least 50% Tobacco

Constituent	Low		High	
	Value	Cigarette	Value	Cigarette
Nicotine	0.70-0.80%	Var. 31	2.83-3.25%	Var. 21
TVB nicotine	0.156%	Var. 31	0.573%	Var. 21
Total phenols	0.93%	Var. 19	3.57%	Var. 1
Nitrate (NO_3-N)	0.11-0.17%	Var. 14	0.60-0.90%	Var. 16
Total fatty acids	1.340 mg/g	Var. 19,20	5.620 mg/g	Var. 22
Phytosterols	0.8561 mg/g	Var. 31	2.1726 mg/g	Var. 12
Lipid residue	114.9 mg/g	Var. 31	328.9-9 mg/g	Var. 21
Waxes	0.28%	Var. 8,26	74.0%	Var. 21
Petroleum ether extract (nonvolatile)	1.9%	Var. 31	5.2%	Var. 21

TABLE 4

High and Low Values of Selected Condensate Constituents[a] for Cigarettes Composed of at Least 50% Tobacco

Constituent	Low		High	
	Value	Cigarette	Value	Cigarette
Nicotine	64.87 mg	Var. 25	174.34 mg	Var. 21
Benzo(a)pyrene	0.82μg	Var. 19	1.45 μg	Var. 26
Phenol	0.48 mg	Var. 25	4.57 mg	Var. 23
pH	4.92	Var. 27	7.53	Var. 19
Total weak acids	1.68 mg	Var. 25	2.40 mg	Var. 15
Fatty acids	8.46 mg	Var. 19	23.75 mg	Var. 10
Neophytadiene	7.11 mg	Var. 27	12.76 mg	Var. 19

High and Low Values of Selected Whole Smoke[b] Constituents for Cigarettes Composed of at Least 50% Tobacco

Constituent	Low		High	
	Value	Cigarette	Value	Cigarette
TPM	1.81 mg	Var. 25	3.84 mg	Var. 1
Nicotine	0.16 mg	Var. 25, 31	0.44 mg	Var. 21
Phenol	3.34 μg	Var. 25	22.38 μg	Var. 9
Acetaldehyde	44.60 μg	Var. 27	143.25 μg	Var. 24
Acrolein	4.48 μg	Var. 23	12.14 μg	Var. 18
Isoprene	22.67 μg	Var. 27	62.84 μg	Var. 21
HCN	5.74 μg	Var. 17	48.82 μg	Var. 21
NO_x	18.51 μg	Var. 27	140.02 μg	Var. 18
CO	0.64 ml	Var. 23	2.18 ml	Var. 24

[a] Per g of dry condensate
[b] Based on delivery/puff

est values of selected leaf constituents for those cigarettes composed of at least 50% tobacco. (The 100% nontobacco cigarettes generally had much lower levels of these constituents, and in many cases the levels of these constituents were so low as to be undetectable.)

2.3 *Smoke and Condensate Analyses*. The results from the condensate and smoke analyses are discussed on pages 49–66. The low and high values for selected constituents are summarized in Table 4, once again for cigarettes composed of at least 50% tobacco.

2.4 *Skin Painting Bioassay*. This section discusses the relative differences among cigarette blends in terms of the numbers of tumors observed during the dorsal skin painting experiments.

Table 5 summarizes the occurrences of tumors and of deaths from nontumorous [1] causes for both high- and low-dose experimental groups painted with cigarette condensate. Table 6 presents a summary of the life-table statistics for the third cigarette experiment based on histopathology data.

Graphical formats of the ranked P_r values, based on histopathologically verified tumor data, are presented in Figure 1 for the 12.5-mg dose level, in Figure 2 for the 25-mg dose level, and in Figure 3 for the 50-mg dose level. The point estimates of the P_r are enclosed within 95% confidence intervals on these figures. Confidence intervals enable the reader to estimate the accuracy of the P_r numerical values, to observe the rankings, and to estimate the extent of significant differences. For example, if the P_r point estimate of one group falls within the confidence interval of a different group, the difference in the two corresponding P_r values is statistically insignificant (at the level of significance dictated by the size of the confidence intervals). On the other hand, if two confidence intervals are disjoint, the difference in point estimates is significant. For the case in which two confidence intervals overlap but neither point estimate falls within the confidence interval of the other, numerical methods should be used in testing for a significant difference.

Negative and vehicle controls. Two groups of 100 mice each were negative controls and two groups of 100 mice each were vehicle (acetone) controls.

	Group No.	*Survival at 546 Days*	*No. of Tumorous Mice*
Vehicle controls	63	66%	0
	64	58%	0
Hair clipped controls	65	63%	0
	66	68%	0

Positive (carcinogen) controls. Groups of 100 mice each received daily doses of 1.25, 2.50, 5.0 μg of benzo[a]pyrene (BaP). Most of the tumors that developed in these positive control animals were carcinomata. Latent periods to tumor were much shorter than those of other experimental groups; most of the mice died before the twelfth month. The results show a strong contrast to the experimental groups.

Amt. of BaP (μg)	*Survival at 546 Days*	T_{75}	*No. of Tumorous Mice*
1.25	15%	402	53
2.50	0%	281	83
5.0	0%	235	91

[1] Nontumorous death is the diagnosis if an animal dies and is necropsied, and histopathologic examination does not find a tumor.

The mean survival rate for these three positive control groups, taken together, is significantly lower than those of the negative control and of the low- and high-dose treatment groups, as expected.

Summary of comparisons among blends. Tables 7 (12.5-mg dose) and 8 (25-mg dose) summarize the statistically significant differences among the P_r values (those based on histopathologically verified tumors) for treatment groups used in the third cigarette experiment. For completeness, each group was compared to all remaining groups. The differences were tested using P_r values and standard errors are listed in Figures 1 and 2.

Each variable showing a significant difference at the 1% level of significance is noted in the tables by a 1 and at the 5% level by a 5. A zero indicates that the difference is not significant at the 5% level or at any lower percent level. A plus sign (+) indicates that the row variable has a larger P_r than the corresponding column variable. A negative sign (−) indicates that the row variable has a smaller P_r than the column variable. The following pages summarize the comparisons among blends using these statistically significant differences based on P_r values with verified data.

TABLE 5

Series III Fate of 6200 Mice Painted with Cigarette Condensate
(Based on Histopathologically Verified Tumor Data)

Variable No.	Low Dose (12.5 mg) P_f[a]	T_m	Σ Tumors[b]	Σ Paps.[b]	Σ Benign Lesions	Σ Dead Animals (No Tumor)	High Dose (25 mg) P_f[a]	T_m	Σ Tumors[b]	Σ Paps.[b]	Σ Benign Lesions	Σ Dead Animals (No Tumor)
1	.792	546	18	11	0	25	.434	264	49	17	1	23
2	.771	546	19	7	0	33	.414	237	51	16	1	25
3 (3.0mg)	.977	546	2	0	0	32	.909	546	2	1	0	43
4	.881	546	11	2	0	29	.477	296	44	8	0	29
5 (3.0mg)	.986	546	1	1	0	25	.938	546	5	1	0	29
6	.824	473	23	16	1	37	.370	253	60	19	4	30
7	.720	540	22	10	0	27	.461	300	44	12	0	30
8	[illegible]	473	20	11	1	21	.483	230	46	17	0	24
9	.700	501	25	14	0	28	.331	262	62	19	2	28
10	.695	498	20	16	2	37	.407	274	60	21	2	24
11	.697	480	23	6	1	23	.413	361	51	19	0	22
12	.716	520	22	9	0	34	.432	414	47	3	1	27
13	.743	525	19	10	1	42	.408	301	41	19	0	44
14	.660	450	23	11	2	31	.378	261	49	23	3	31
15	.710	496	22	11	0	40	.594	438	31	11	0	42
16	.851	546	12	10	0	27	.651	463	36	7	1	31
17	.647	477	29	16	0	23	.456	402	46	21	0	25
18	.778	546	18	10	0	34	.564	452	36	12	1	32
19[c]	.626	482	24	13	0	30	.509[c]	272	40	6	0	36
20 (3.0mg)	.976	546	2	2	0	32	.946	546	12	6	0	34
21[c]	.808	[illegible]	28	14	1	30	.532[c]	417	36	12	0	38
22	.747	500	22	3	0	23	.497	260	42	16	0	24
23	.801	546	16	3	0	38	.434	276	49	14	0	24
24	.702	522	24	16	0	37	.294	323	58	18	1	27
25	.734	546	20	7	0	34	.298	237	60	23	1	21
SEB III[c]	.711	505	91	30	2	144	.449	276	104	56	4	103

	Low Dose (25 mg)						High Dose (50 mg)					
26	.557	424	30	17	1	27	.279	361	60	17	1	38
27	.561	420	36	8	3	23	.305	358	66	13	1	30
28	.290	[illegible]	64	20	2	30	.120	301	74	19	1	17
29	.404	430	42	10	0	26	.160	304	70	12	0	21
30	.041	[illegible]	82	16	0	17	.060	275	70	14	1	30
31	.271	[illegible]	61	16	2	25	.190	340	20	12	1	58

[a] P_T is the estimated probability of tumor avoidance in the experiment; T_{75} is the estimated number of days on experiment until 75% of the treated mice would be expected to be tumor free.

[b] Σ Tumors = Σ papillomas + Σ other malignancies.

[c] Both dose groups for variables 19 and 21 are at the 12.5-mg level.

[d] SEB III consists of variables 4, 6, 7, 8.

TABLE 6

Cigarette Condensate Study, Third Experiment, Final Probability of Survival Using Histopathologically Verified Tumor Data

Variable No.	Group No.	Description	Response: Low Dose (12.5 mg) Tumors	Deaths	P_r	T_m	High Dose (25 mg) Tumors	Deaths	P_r	T_m
1	35,36	University of Kentucky Reference (1R1)	13	25	.7916	646	49	23	.4341	364
2	47,48	SEB I	19	33	.7706	646	51	25	.4139	337
3	25,26	SEB I (3 mg, 6 mg)	2	33	.9769	646	2	43	.9894	646
4	51,52	SEB III	11	29	.8607	646	44	29	.4770	376
5	17,18	SEB III (3 mg, 6 mg)	1	35	.9857	646	5	29	.9379	646
6	7,8	SEB III	28	37	.6342	473	50	29	.3760	293
7	53,54	SEB III	22	37	.7392	640	44	30	.4614	300
8	29,30	SEB III	30	31	.6004	473	46	24	.4027	338
9	23,24	SEB III with low-porosity paper (5 cm/min)	25	28	.7093	601	62	28	.3307	302
10	19,20	SEB III with high-porosity paper (60 cm/min)	30	37	.6149	436	60	24	.4070	374
11	37,38	SEB III with very high porosity paper (100 cm/min)	33	29	.6065	469	61	22	.4124	363
12	33,34	SEB III with no sugar	22	34	.7150	529	47	27	.4321	414
13	9,10	SEB III with no humectant	19	43	.7428	528	41	44	.4083	303
14	5,6	SEB III with powdered cocoa	28	31	.6692	460	49	31	.3763	364
15	41,42	SEB III with no sugar, no humectant	22	40	.7056	406	31	42	.5935	438
16	57,58	SEB III with LAN additive #1	12	27	.8606	646	35	31	.5610	403
17	13,14	SEB III with LAN additive #2	29	28	.6470	477	45	26	.4646	402
18	55,56	SEB III with LAN additive #3	18	34	.7777	646	36	32	.5640	452
19	31,32	SEB III burley blend with sugar (12.5 mg, 12.5 mg)	34	30	.5658	452	40	36	.5057	372
20	15,16	SEB III burley with sugar (3 mg, 6 mg)	2	32	.9764	646	13	34	.8478	646
21	3,4	SEB III burley blend with no sugar (12.5 mg, 12.5 mg)	28	30	.5876	420	36	38	.6324	417
22	61,62	SEB III with dilution filter	22	28	.7469	608	42	24	.4568	309
23	59,60	SEB III with dilution filter and very high porosity paper (100 cm/min)	16	36	.8089	646	49	24	.4336	376
24	43,44	SEB III with cellulose acetate filter	24	37	.7022	622	58	27	.2936	323
25	21,22	SEB III with permanganate filter	20	34	.7236	646	60	21	.2961	337
SEB III	91,92	SEB Variables 4, 6, 7, 8 combined	91	144	.7112	616	184	113	.4494	376
			Low Dose (25 mg)				High Dose (50 mg)			
26	27,28	ATS-A & SEB III 30/70 with flavor	38	27	.5574	424	50	28	.2796	361
27	45,46	ATS-A & SEB III 30/70 with high-porosity paper (60 cm/min) dil. fil. & flavor	36	33	.5606	429	56	30	.3080	368
28	1,2	ATS-B 100% (old material, old dyes)	64	30	.2566	306	74	17	.1332	301
29	49,50	ATS-B 100% (new material, no dyes)	42	36	.4038	439	70	21	.1498	301
30	11,12	ATS-B 100% (old material, no dyes)	52	17	.0407	208	70	30	.0000	275
31	39,40	ATS-B (old material, no dyes) & SEB III 50/50	61	26	.3714	232	39	58	.1897	349

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Veh. control	63,64	Acetone	0	77	1.0000	646
Neg. control	65,66	Hair clipped only	0	67	1.0000	646
BaP	67	Benzo[a]pyrene (1.25 µg)	53	22	.2767	402
BaP	68	Benzo[a]pyrene (2.50 µg)	82	17	.0000	281
BaP	69	Benzo[a]pyrene (5.00 µg)	91	9	.0000	236

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RJR SECRET No. 243 By [handwritten initials]

October 20, 1978

Dr. A. H. Laurene

Subject: Recommendations re Coumarin Use

RECOMMENDATIONS

1. Despite the listing of coumarin as a Category 1 chemical that may be regulated under the OSHA proposed generic carcinogen policy, it is recommended that the use of coumarin at levels less than 0.06% on Company products be continued.

   Evidence indicates:

   a. Coumarin has been reported in tobacco and in the smoke from tobacco not top dressed with added flavorants.

   b. Coumarin-treated cigarette tobacco does not yield the anticoagulant dicoumarol in either mainstream or sidestream smoke.

   c. Coumarin has been examined in a non-tobacco industry lab for mutagenicity with four Salmonella strains and found to be nonmutagenic.

   d. Coumarin is not carcinogenic to rats at or below feeding levels of 50 mg/day; contradictory results have been obtained at feeding levels higher than 50 mg/day.

   e. When body weight is considered, a rat fed coumarin at the noncarcinogenic level up to 50 mg/day is exposed to 35,000 times the dose to which a pack-a-day smoker of a high-coumarin delivery cigarette (NOW) is exposed. Usually an exposure ratio of 200 to 300:1 is considered an adequate safety factor.

2. It is recommended that at least one major competitive brand (presently containing coumarin) be monitored quarterly for coumarin content to determine whether competitive users desist from coumarin use. (All domestic companies except PM add coumarin to one or more of their cigarette products.)

3. It is also recommended that the air in areas where coumarin-containing flavor formulations are prepared be monitored by Research personnel during flavor formulation to ascertain the coumarin level in the workplace. The level found will dictate subsequent action re lunchroom facilities, medical surveillance.

4. It is recommended that PR statements concerning Category 1 chemicals in general and coumarin in particular be monitored by R&D personnel.

Source: https://www.industrydocuments.ucsf.edu/docs/tggl0001

MEMORANDUM

In my previous memo (July 7, 1978), I recommended the continued use of coumarin at appropriately low levels for flavoring purposes in RJR products. Shortly thereafter, OSHA issued a tentative list of chemicals that may be regulated under its proposed generic carcinogen policy [Summarized in CHEM. ENG. NEWS, 29 (July 31, 1978)]. Category I of this list contained coumarin. To be placed in Category I, a chemical must be shown to be carcinogenic either in two mammalian species or in one species if the tests have been replicated. Coumarin falls under the latter qualification.

Baer and Griepentrog [MED. ERNAHR., 8, 244-251 (1967)] fed groups of rats in a 1.5-year chronic feeding study a diet to which coumarin had been added in concentrations of 0.1, 0.25, 0.5, or 0.6%. At the daily feeding level (20 g/day) each animal in the group received 20, 50, 100, or 120 mg of coumarin per day, or 50, 125, 250, or 300 mg of coumarin per kg body weight per day, respectively, for the duration of the experiment. At the two lower levels, no tumors were observed; at the two higher levels, liver carcinomata resembling bile duct carcinomata were observed. These results do not agree with those in an FDA study by Hagan et al. [TOXICOL. APPL. PHARM., 5, 141 (1967)] in which no tumors were observed in rats at the 0.5% coumarin feeding level (100 mg/day).

In 1973, Griepentrog [TOXICOLOGY, 1, 93-102 (1973)] reported the results of a study in which he fed groups of rats over a 2-year period a diet to which coumarin had been added in concentrations of 0.1, 0.25, 0.5, and 0.6%. The latter two groups showed liver carcinomata, again contrary to the FDA study by Hagan et al.

For the sake of discussion and because no tumors were observed at this level, I will consider only the 50 mg/day dose of coumarin fed to each rat in its food. How does this daily dose administered to the rat compare with a smoker's exposure to coumarin in the smoke from a pack of cigarettes? Table I summarizes coumarin data for various competitive brands over the past several years. Only PM does not use this flavorant in its cigarettes.

If we assume 20% transfer (this is a high transfer) of coumarin from the tobacco to the mainstream smoke, the daily exposure per pack of NOW cigarettes containing relatively high levels of coumarin (~67 μg/g of tobacco) is about 67 x 0.2 x 20 or 268 μg of coumarin per day, the rat:smoker exposure ratio under these conditions is 50 mg/268 μg or 187. This does not take into account the body weight difference between the hosts. If exposure level per kg body weight is considered and the rat and human weights are assumed to be 0.4 and 75 kg, respectively, the rat:smoker exposure ratio is (50 x 1000/0.4)/(268/75) or about 3.5×10^4. For two packs of NOW/day, this ratio is halved to about 1.75×10^4. For cigarettes such as the VANTAGE and the WINSTON, the ratios will be substantially greater.

The massive dose of coumarin used in the rat feeding experiments described above is reminiscent of the massive dose of saccharin alleged to have produced bladder tumors when fed to mammals. The dose levels in the animal experiments for both the saccharin and the coumarin cases are, in my opinion, entirely unrealistic.

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REGULATION OF TOBACCO PRODUCTS
(Part I)

HEARINGS

BEFORE THE

SUBCOMMITTEE ON
HEALTH AND THE ENVIRONMENT

OF THE

COMMITTEE ON
ENERGY AND COMMERCE
HOUSE OF REPRESENTATIVES

ONE HUNDRED THIRD CONGRESS

SECOND SESSION

MARCH 25 AND APRIL 14, 1994

Serial No. 103–149

Printed for the use of the Committee on Energy and Commerce

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Statement of R. J. Reynolds Tobacco Company

R.J. Reynolds Tobacco Company ("Reynolds Tobacco") welcomes this opportunity to respond to the inaccurate and misleading attacks that have precipitated these hearings. For the past several weeks, Reynolds Tobacco and the rest of the tobacco industry have been bombarded with spurious and inflammatory claims. Our responses to these charges are simple and straightforward:

- Does Reynolds Tobacco add nicotine to its products? No.
- Does Reynolds Tobacco manipulate nicotine yields to create, maintain, or satisfy "addiction"? Again, the answer is no.
- Does Reynolds Tobacco hold patents for technology that relates to modification of nicotine yields independent of "tar" yields? Yes. In fact, for years some governments, smoking and health critics, and international public health scientists have encouraged such developments in cigarette design.
- Is Reynolds Tobacco using such technology commercially? No.
- Is cigarette smoking an "addiction"? No, cigarette smoking is not an "addiction" under any meaningful definition of the term, including the new definition presented by Dr. Kessler before this Subcommittee.

There is no factual or policy basis to regulate or ban cigarettes as drugs simply because they contain nicotine or simply because cigarette manufacturers have the ability to reduce the nicotine yields of their products. This company is not engaged in some sinister plot to deceive the American smoker.

Progress or Prohibition

If this Subcommittee fairly and objectively evaluates the true facts about cigarette design, it must find that the efforts of Reynolds Tobacco and others in the industry demonstrate a remarkable record of achievement and progress. This company is justifiably proud of those accomplishments and of the dedicated and talented employees who have

contributed and now contribute to them. We regret that others seek to advance an agenda of prohibition over progress.

Today, we are here to discuss whether there is a basis for FDA regulation of cigarettes as drugs. Contrary to many reports, this issue is not novel. In fact, the question has been advanced and rejected many times before. For example, twenty-two years ago, the Commissioner of the Food and Drug Administration (FDA), Dr. Charles C. Edwards, testified at a hearing similar to this one before the Consumer Subcommittee of the Senate Committee on Commerce. Dr. Edwards stated, "Cigarettes and other tobacco products would be drugs subject to the Federal Food, Drug and Cosmetic Act if medical claims are made for the product . . . . However, cigarettes recommended for smoking pleasure are beyond the Federal Food, Drug, and Cosmetic Act."[1] Dr. Edwards was echoing a conclusion that has been consistently reached -- both by FDA and the courts prior to and after his statement.[2]

Three weeks ago, FDA Commissioner Dr. David Kessler appeared before this Subcommittee and testified extensively concerning the "task facing the FDA," which he characterized as "to determine whether nicotine-containing cigarettes are 'drugs' within the

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[1] To Amend the Federal Cigarette Labeling and Advertising Act to Require The Federal Trade Commission to Establish Acceptable Levels of Tar and Nicotine Content of Cigarettes, 1972: Hearings on S.1454 Before the Consumer Subcomm. of the Senate Comm. on Commerce, 92nd Cong., 2d Sess. 239 (1972) (statement of Charles C. Edwards, Comm., FDA).

[2] See, e.g., FTC v. Liggett and Myers Tobacco Co., 108 F.Supp. 573 (S.D.N.Y. 1952), aff'd on op. below, 203 F.2d 955 (2d Cir. 1953); Letter from Donald Kennedy, Commissioner of Food and Drugs, to John F. Banzhaf, III, Dkt. No. 77P-0185 (December 5, 1977); Action on Smoking & Health v. Harris, 655 F.2d 236 (D.C. Cir. 1980).

meaning of the Federal Food, Drug, and Cosmetic Act." All cigarettes sold are "nicotine-containing cigarettes," and indeed the tobacco plant is known as nicotiana tabacum in recognition of the fact that it naturally contains nicotine. Moreover, the facts relevant to whether FDA has jurisdiction over cigarettes today are substantially the same as when Dr. Edwards testified in 1972 and when the FDA rejected petitions to regulate cigarettes in 1977 and on other occasions. At those times, as is the case today, a variety of cigarette brands was available to consumers which yielded a variety of "tar" and nicotine levels. Through advances in cigarette design and in response to consumer preferences, however, the average cigarette sold today yields one-third less "tar" and nicotine than when Dr. Edwards testified.

Cigarette Design

How and why have these reductions in "tar" and nicotine yields come about? To evaluate these questions completely, it is imperative to consider the evolution in the design of cigarettes over the last forty years -- an evolution that, in its purpose and effect, differs significantly from the grossly inaccurate allegations and misrepresentations by our critics in these proceedings and recently in the press. In short, Reynolds Tobacco designs cigarettes to respond to consumer demand and to attempt to address the many scientific and other criticisms that have been leveled at our products for more than forty years. Today's cigarettes reflect the enormous efforts to respond directly to consumer demand and those criticisms and suggestions. A very brief discussion of the history of cigarette design will illustrate why these recent claims are misguided.

Early cigarettes were primarily cut tobacco (much like pipe tobacco) wrapped in paper, with flavorings such as the oil of citrus peels. The quality of a cigarette depended

primarily on the single type of tobacco it contained -- Turkish tobacco was used in premium cigarettes and domestic air-cured or flue-cured tobacco was used in less expensive cigarettes. The first American blend cigarette, which combined both Turkish and domestic tobacco, was Reynolds Tobacco's Camel brand, introduced in 1913. Although slightly different blends and different materials were used in cigarette manufacturing, cigarettes remained largely unchanged until the early 1950s.

At that time, most cigarettes produced in the United States were made from flue-cured, burley and Turkish tobaccos. They were 70 mm long and unfiltered. When smoked, these cigarettes yielded an average of 40 mg of "tar" and 2.8 mg of nicotine by methods comparable to those used by the United States Federal Trade Commission (FTC). (The FTC methods became official in 1969).

A number of watershed developments in the early 1950s led to another evolution in cigarette design. Several epidemiologic studies published during the early 1950s reported that there was a statistical association between cigarette smoking and lung cancer. Also, in 1953, Dr. Ernst Wynder and others published the results of a mouse skin painting experiment in which the researchers observed skin tumors on the backs of mice exposed to cigarette smoke condensate. All these studies were widely publicized in the general media and the media coverage affected consumer demand. Reynolds Tobacco in turn has made extensive efforts to respond to these scientific theories and demands and the tastes of its consumers to produce a broad array of products.

Since the 1950s, Reynolds Tobacco, among many other lines of research, has pursued two basic lines of research and development in this area: (1) identification of individual

constituents in tobacco smoke and development of technology to attempt to reduce or remove those of potential concern, and (ii) development of new technologies to reduce yields of "tar" and nicotine generally. The first line of research has had limited success; the second line of research has been remarkably successful.

Selective Reduction

During the 1950s and early 1960s, many researchers focused on one chemical constituent of smoke (or a family of constituents) in the search for a "cancer-causing" agent that would explain the epidemiologic and skin painting results. This focus turned to disappointment, as reflected in the 1964 Report of the Advisory Committee to the Surgeon General ("Surgeon General's Report"). From the mid-1950s until today, a succession of constituents has been targeted by the biomedical community. Even today, however, the biomedical community has been unable to agree on which, if any, of those constituents is responsible for the reported association between cigarette smoking and lung cancer.

Cigarette manufacturers and others explored and published numerous methods to reduce or eliminate individual constituents (or a family of constituents) in cigarette smoke, e.g. reducing the temperature at which the cigarettes burned, breeding tobacco plants to change the chemical composition of the tobacco, and adding different types of filters or other filtration mechanisms to the cigarette. Unfortunately, manufacturers faced a moving target as the focus changed from constituent to constituent. Constituents of concern at one point in time were later determined by the scientific community to be of no significance. Moreover, techniques that might have selectively reduced a constituent in the laboratory

commonly increased another constituent. In general, efforts to reduce individual constituents have not been successful.

General Reduction

During the same period, Reynolds Tobacco and other cigarette manufacturers also directed their research to attempt to reduce levels of all constituents. This approach, also advocated by researchers such as Dr. Ernst Wynder, offered advantages over selective reduction because it led to the reduction of total smoke yields and the levels of individual compounds more or less proportionately.

To understand the concept of general reduction, it is essential to understand what smoke is. Smoke is a complex mixture -- it consists of a particulate or "tar" phase as well as a vapor or gas phase. Since the mid-1950s, cigarette manufacturers have devoted extensive resources to achieve a general reduction in "tar" and the vapor phase components of cigarette smoke. Techniques incorporated in cigarettes over the last 40 years which reduce "tar" include:

- Filtration
- Reconstituted tobacco
- Paper porosity
- Reduced tobacco
- Expanded tobacco
- Filter ventilation

Design changes such as the development of more porous cigarette paper, improved filtration, and the use of expanded (or "puffed") tobacco and reconstituted tobacco made

general reduction possible. By utilizing one or more of these techniques, cigarette manufacturers can offer smokers a variety of cigarettes with a range of "tar" and nicotine levels. Cigarette designers have been so successful in their efforts to respond to the demand for these reductions that today there are commercially available cigarettes that yield "tar" and nicotine at levels so low they cannot be measured reliably by the FTC's standard procedure.[3] In 1979, the Surgeon General listed more than 25 different design techniques that reduce yields of "tar" and nicotine.[4] Each of these techniques has been well-publicized and known to the government, public health, scientific and even lay communities. A brief analysis of these design achievements demonstrates the effectiveness of general reduction methods to achieve lower yields of "tar" and other smoke constituents.

The earliest developments included the cellulose acetate filter, use of porous paper, and use of reconstituted tobacco. Each of these developments was in place by 1965, and "tar" and nicotine yields had been reduced dramatically. After 1965, the principal design

[3] See, e.g., Federal Trade Commission, "Tar," Nicotine and Carbon Monoxide in the Smoke of 207 Varieties of Domestic Cigarettes 2-3 (1985).

[4] Public Health Service, U.S. Department of Health, Education, and Welfare, Smoking and Health: A Report of the Surgeon General 14:110 (1979) ("1979 Surgeon General's Report"). The techniques identified in the 1979 Surgeon General's Report were genetics and breeding of tobacco plants, planting density, nitrate fertilization, applying agricultural chemicals, topping the tobacco plant at different stages, altering the type of tobacco, altering the position of the stalk, changing the nitrate content, selecting tobacco with specific constituents (e.g., proteins, carbohydrates, resins), curing, homogenized leaf curing, grading, fermentation, solvent extraction, tobacco expansion (freeze-drying), additives, blending, changing the amount of tobacco, changing the amount of tobacco stems, utilizing varying amounts of reconstituted tobacco, using expanded tobacco, varying the tobacco cut, using porous cigarette paper, perforating the cigarette paper, smoke filtration, and perforating the filter tips. Id. at 14:108-14.

breakthroughs were expanded tobacco and air dilution through perforation of cigarette filters. Expanded tobacco resulted from the search for ways to reduce the volume of tobacco in each cigarette in order to reduce "tar" and nicotine yields. The tobacco is "puffed" or expanded in order to allow the same amount of tobacco to occupy more space, much like popping popcorn. As a result, each cigarette is filled with less tobacco, there is less tobacco available to be burned, and the yields of "tar" and nicotine are therefore reduced. Reynolds Tobacco developed expanded tobacco and was the first to introduce it commercially, in 1968. In fact, Reynolds Tobacco licensed this process to others in the industry for commercial use throughout the world.

In the late 1960s, scientists discovered that perforating the cigarette filter allows air to mix with the mainstream smoke, thereby diluting the smoke and reducing the total yields of "tar," and nicotine. Air dilution also reduces the burning temperature of tobacco and causes less tobacco to be burned per puff, thereby further reducing the "tar" and nicotine yields. Perforated filters were first sold commercially in about 1972. By 1981, approximately 50% of all cigarette brands sold had perforated filters.[5]

By 1981, the tobacco content by weight of the average cigarette had declined by 23.8% through the use of expanded tobacco.[6] In some ultra low-"tar" brands, expanded

[5] Public Health Service, U.S. Department of Health and Human Services, The Health Consequences of Smoking: The Changing Cigarette, A Report of the Surgeon General 209-10 (1981) ("1981 Surgeon General's Report").

[6] Id. at 209-10.

tobacco was used to a much greater extent to reduce the weight even more dramatically.[7] Thus, as part of the design techniques to achieve lower yields of "tar" and other smoke constituents, the amount of tobacco in cigarettes has been reduced, with the corresponding result that the smoke nicotine has also been reduced dramatically.

The cigarette design efforts discussed above have been reviewed and commended by government and other scientists. For example, from 1966 through 1978, the National Cancer Institute supported a program to develop a "less hazardous cigarette". This effort involved government, tobacco industry, public health groups, and universities. Reynolds Tobacco and other cigarette manufacturers participated in this program. The NCI program evaluated over 100 different cigarette designs -- many of which had already been incorporated in commercial cigarettes by the major manufacturers. The results of this program indicated that the general reduction approach as described above was the best approach to respond to the scientific criticisms of cigarettes. Importantly, virtually every design variable that was evaluated by the NCI group had been developed by the United States tobacco industry and utilized in a commercial brand.

In 1979, scientists involved in the field of smoking and health came together at the Banbury conference. This conference reviewed virtually all work that had been done to modify cigarettes during the previous twenty-five years in response to the smoking and health controversy. All of the papers presented at the Banbury conference were published,

[7] This point is especially significant because it addresses Dr. Kessler's "surprise" at finding that, for some brands in the ultra low-"tar" category, the percent nicotine in the tobacco itself might be the same or slightly higher than the percent nicotine in the tobacco used in higher-yield cigarettes. Reducing the amount of tobacco has a major influence on the nicotine yield to the smoker.

together with all the debate and discussions. The consensus among scientists participating in that program was that overall "tar" and nicotine reduction was the most effective and most appropriate approach. Several scientists, including Dr. Dietrich Hoffmann, acknowledged the responsiveness of the tobacco industry:

> I do think the tobacco industry, voluntary or not, adjusts very well to the demands of the logical reasoning of the scientific community and that we should continue on this path.[8]

In Dr. Kessler's March 25, 1994 statement, he asked the cigarette companies to address the intent of cigarette design developments. The clear intent behind cigarette design developments has been and remains to manufacture and market a broad range of cigarette products in response to the demands and tastes of today's adult smokers and to ensure cigarette to cigarette and pack to pack consistency within a brand. Within the universe of cigarette products, there is a range of "tar" and nicotine levels. As noted earlier, reducing "tar" yields automatically results in roughly proportional reductions in nicotine yields. That is seen by the dramatic reduction in both "tar" and nicotine achieved by Reynolds Tobacco and other cigarette manufacturers since 1955.

In 1957, Dr. Ernst Wynder and others called for efforts to reduce "tar":

> [F]or practical purposes, a filter-tip capable of filtering out 40 percent of the tar would be a step in the right direction .... "Such a filter-tip . . . placed on a regular-size cigarette which normally yields 30 milligrams of tar in its smoke, would reduce the smoker's tar exposure to about 18 milligrams. A reduction to that level, as shown both by animal experiments and human

[8] Dietrich Hoffmann, Discussion in "Risk Reduction Achievements", Banbury Report 3 - A Safe Cigarette?, pp. 155-178 at 174 (1980).

statistical studies would be a significant reduction in cancer risk."*

The tobacco industry has accomplished this objective -- and has gone much further. The vast majority of today's cigarettes are 85-100 mm long, have filters and yield an average of 11.5 mg of "tar" and 0.8 mg of nicotine. Some cigarettes now available yield less than 1.0 mg of "tar" as measured by the FTC method.

These "tar" and nicotine reductions have largely been achieved through innovations in cigarette design -- innovations pioneered by Reynolds Tobacco and other members of the tobacco industry. Since the complexity of smoke provides a cigarette with its taste and other sensory properties, many of these reductions in "tar" and nicotine have come at the expense of flavor. Some smokers are unwilling to sacrifice flavor for reduced "tar." This has prompted a continuing effort to develop new cigarette designs.

It is ironic that in the face of the overwhelming recommendations of just such an approach, certain public and private critics of cigarettes have decided once again to attack the industry -- and to seek to stop, if not to reverse, the extensive design innovations that other public and private critics have encouraged over the years.

"Tar"/Nicotine Ratios

Reynolds Tobacco does not manipulate the nicotine in its products to create, maintain, or satisfy "addiction". Claims to that effect are false. As "tar" yields have been reduced over the years, nicotine yields have also been reduced, roughly in proportion to the "tar." The fact that "tar" to nicotine ratios are not exactly the same for all cigarettes is not

* Mattox, L. and Monahan, S., "Wanted -- And Available -- Filter-Tips That Really Filter", Readers Digest, pp. 43-49, 44 (August 1957) (quoting Dr. E.L. Wynder).

news to anyone familiar with tobacco products or to anyone who has reviewed the extensive "tar" and nicotine reports published by the FTC.

Reynolds Tobacco's cigarettes contain approximately one and one-half to two and one-half percent nicotine, depending upon the tobacco blend. When burned, these cigarettes yield varying amounts of "tar" and nicotine. "Tar" to nicotine ratios, while not constant, are very closely linked because both are found in the particulate phase of smoke. As "tar" yield is reduced, through filtration, paper porosity, expansion, and other design parameters, nicotine yield is also reduced. Filters, however, are slightly more efficient at reducing "tar" yield than nicotine yield. This is due to the fact that cellulose acetate, the primary filter material used by Reynolds Tobacco and others, was developed to reduce "tar" yield. The ability of these filters to reduce the gas phase constituents is somewhat limited. Since a small amount of nicotine (unlike "tar") is found in the gas phase of cigarette smoke, as well as in the particulate phase, slightly more "tar" is filtered out of the smoke, proportionately, than nicotine. Thus, as yields are reduced, the ratio of "tar" yield to nicotine yield is reduced slightly.

In response to the fact that "tar" and nicotine yields are so closely and naturally linked in cigarette smoke, many public health officials and others have suggested that the tobacco companies should attempt to develop cigarettes which break that link. In other words, we have been encouraged to develop cigarettes with reduced "tar" while maintaining nicotine yields. Notable among officials who have encouraged such development is the Independent Committee on Smoking and Health of the United Kingdom, which recommended in 1983 that ". . . there should be available to the public some brands with

low levels of tar and a proportionately higher nicotine yield."[10] According to one recent publication cited by Dr. Kessler in his testimony:

> One proposal has been to develop tobacco that is high in nicotine but low in tar. This is not easy to do naturally; nicotine and tar are highly correlated in the tobacco leaf. One method would be to add nicotine to a low tar, low nicotine cigarette.[11]

The fact is many scientists, government and/or public health officials have suggested reducing "tar" to nicotine ratios as a way toward potential progress in cigarette design.[12]

Much as the industry responded to calls to reduce "tar" and nicotine yields in the 1950s and 1960s, Reynolds Tobacco has devoted research to responding to these calls to reduce the "tar" to nicotine ratios. Out of the hundreds of patents issued to Reynolds Tobacco personnel over the years, Dr. Kessler referred to nine Reynolds Tobacco patents during his recent testimony to this Subcommittee. These patents reflect work that Reynolds has done in this area. As Dr. Kessler recognized, however, patents do not necessarily reflect what is being used in practice. While Reynolds Tobacco has been able to develop a cigarette which disassociates "tar" and nicotine in the laboratory, it has not been able to achieve an acceptable commercial product. As stated above, this is not easy to do because

[10] Third Report of the Independent Scientific Committee on Smoking and Health of the United Kingdom (1983).

[11] Schelling, T.C., "Addictive Drugs: The Cigarette Experience." Science Vol. 255:430-433 (1992).

[12] See, e.g., "UICC Tobacco Control Fact Sheet 3," Tobacco and Cancer Programme, International Union Against Cancer (March 1993); Editorial, "Monsieur Nicot's Legacy," Lancet II (8249): 763 (1981); Russell, M.A.H., "Smoking and Society (There Is No Question)". Rehabilitation, 32 (1-4): 41-42 (1979).

"tar" and nicotine are so highly correlated. If we could develop such a cigarette acceptable to the consumer, it would apparently be welcomed and encouraged by European governments and public health officials, rather than being characterized as some sinister plot by tobacco companies, as Dr. Kessler appears to characterize it.[13] In fact, none of the nine Reynolds Tobacco patents cited by Dr. Kessler has been used commercially.

Published FTC "Tar" and Nicotine Yields

The amount of nicotine present in a cigarette is in large part a result of the choice of tobaccos used in the cigarette blend, which are chosen because of their taste and other properties.[14] It is not present as a result of a decision to "manipulate" nicotine levels to some carefully controlled "addictive level." The concept of an "addictive level", raised but not defined by Dr. Kessler, is not a concept known to or understood by Reynolds Tobacco. Neither that concept nor any similar concept is used by Reynolds Tobacco in the design of its cigarettes. We do not know what the concept means, and we are unaware of any data

[13] In 1988, Reynolds Tobacco introduced Premier, a cigarette that heated rather than burned tobacco. That cigarette addressed many of the scientific criticisms that had been made against cigarettes for many years. It virtually eliminated "tar"; it vastly reduced environmental tobacco smoke; and it reduced cigarette ignition propensity. Despite these attributes, certain U.S. government officials, public health officials and, of course, anti-smoking activists launched a vigorous attack on the cigarette -- in terms that sound strikingly similar to the anti-smoking rhetoric surrounding this current debate. European health officials, on the other hand, and some United States scientists recognized the attributes of Premier and, indeed, encouraged the development of similar cigarette technologies. See, e.g., "Smoking Pleasure Without the Danger of Fire and Risks To Health," Die Neu Aerztliche (December 19, 1988); Hoffmann, D., et al., "Cancer of the Upper Aerodigestive Tract: Environmental Factors and Prevention," Journal of Smoking-Related Diseases 3(2): 109-129 (1992).

[14] A variety of agricultural factors and practices influence these properties, including, for example, tobacco type, stalk position of the leaf, curing practices, and crop year.

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that give it meaning. Further, what is relevant is not what is present in the cigarette, but what is present in the smoke.

Dr. Kessler has made much of the fact that the FTC numbers do not necessarily reflect the precise "tar" and nicotine yields for every smoker. This is certainly true, just as EPA mileage estimates do not reflect the precise fuel economy that will be achieved by every automobile driver. The important point is that in spite of broad variations in how individual smokers may smoke any given cigarette, the fact remains that the lower the yield by FTC numbers, the lower the yield will be to any given smoker. The yield for any given smoker will probably be different from the FTC yield; for some smokers it will be higher, for some it will be lower, but overall, the FTC yields are generally predictive of the yield to smokers as a group. The statement, however, that "in reality" low yield cigarettes do not yield low "tar" and nicotine, is not true. In work published by members of the Swiss Federal Institute of Technology, lower yield cigarettes were associated with reduced smoke absorption.[15]

Another indication of Dr. Kessler's misunderstanding of cigarettes relates to his statements concerning low "tar" cigarettes. He stated that from 1967 to 1978 eighteen brands of filter cigarettes underwent increases in overwrap width, resulting in less tobacco being smoked by machine smoking in accordance with the FTC method. Since the FTC method specifies that the cigarette is smoked to within 3 millimeters of the tipping overwrap, and Dr. Kessler stated that the tobacco within the overwrap was still smokeable

[15] Hofer, et al., "Nicotine Yield as Determinant of Smoke Exposure Indicators and Puffing Behavior." Pharmacology Biochemistry and Behavior, Vol. 40, 139-149 (1991).

(and would be smoked by the consumer), he concluded that these brands deviously "cheat" the FTC method. That is not true. First, Reynolds Tobacco uses standard tipping overwrap and has not increased the width because that would reduce puff count and the value to our consumers. But, more importantly, the tipping overwrap simply is not smokeable. No smoker would consciously smoke the overwrap more than once. The tipping paper, because it is not intended to be smoked, imparts a significant off-taste to the cigarette smoke.

Finally, in his testimony before this Subcommittee, Dr. Kessler used several charts (which have since been widely publicized) to support his contention that the nicotine/tar ratio for the lowest "tar" cigarettes has increased since 1982 on a sales weighted basis. This allegation surprised Reynolds Tobacco as much as it surprised Dr. Kessler. Company scientists immediately tried to duplicate Dr. Kessler's charts, using the identical FTC data and the only publicly-available brand sales data of which this company is aware. Despite applying the same data allegedly employed by Dr. Kessler's staff, our scientists cannot duplicate these findings. In fact, our results show exactly the opposite -- nicotine yields and nicotine/"tar" ratios in the lowest "tar" category decreased slightly between 1982 and 1991 -- the time period covered by Dr. Kessler's charts. We have, in fact, asked FDA staff members to provide its data and complete methodology. We would welcome the opportunity to review the data and methodology used by FDA staff to prepare these charts, so that we would have a full opportunity to understand and review the procedures used and evaluate the conclusions reached.

The "Addiction" Hypothesis

A major premise of the charges against the cigarette industry today is the claim that cigarettes are "addictive". Dr. Kessler and our other critics rely on selective and incomplete evidence to support this claim. They ignore significant and meaningful differences between cigarettes and truly "addictive" drugs. When long-established criteria for labeling a substance or activity as "addictive" do not permit our critics to fit cigarette smoking nicely within the existing criteria, these critics resort to a simple tactic to further their agenda -- they attempt to lower the standards and change the definition of "addiction" and its alleged components.

In 1964, the Advisory Committee to the Surgeon General recognized that cigarette smoking did not meet well-established criteria for "addiction."[16] In 1988, the Surgeon General altered the definition to fit the existing data on smoking. In essence, the Surgeon

[16] The 1964 Advisory Committee Report to the Surgeon General defined "addiction" as follows:

> "a state of periodic or chronic intoxication produced by the repeated consumption of drug (natural or synthetic) whose characteristics include:
>
> "(1) An overpowering desire or need (compulsion) to continue taking the drug and to obtain it by any means;
>
> "(2) A tendency to increase the dose;
>
> "(3) A psychic (psychological) and generally a physical dependence on the effects of the drug;
>
> "(4) Detrimental effect on the individual and on society"

The Report concluded that tobacco smoking was properly classified as a habituation. 1964 Surgeon General's Report, 351, 354.

General moved the goalposts after he located the ball on the field. We categorically reject the claim that cigarettes are "addictive", and we know that an objective review of the facts and science supports our position.

Dr. Kessler defined "addiction" in terms of four elements:

- compulsive use
- psychoactive effect
- reinforcing behavior
- withdrawal symptoms

When each of these elements is carefully analyzed in an unbiased manner, it becomes clear that cigarette smoking is no more "addictive" than coffee, tea or Twinkies.[17] Further, in spite of the efforts to expand the definition, it still does not properly encompass cigarette smoking.

1. Compulsive use. This concept of compulsive use, like the definition of "addiction" itself, has undergone a redefinition in an attempt to encompass cigarette smoking. The classic definition of "addiction", as used in the 1964 Surgeon General's Report, properly defines compulsive use seen with hard drug addiction as "an overpowering desire or need (compulsion) to continue taking the drug and obtain it by any means." This is precisely what is seen with truly "addicting" substances like cocaine and heroin. The

[17] Using similarly vague definitions, researchers claim to have discovered addiction to love, jogging, television, credit cards and even eating carrots. See, e.g., Peele, S., Love and Addiction, 1976; Hailey and Bailey, "Negative Addiction in Runners," (1979); Winn, M., The Plug In Drug (1977); Parade Magazine, April 5, 1987, p. 28; Wright, M.R., "Surgical Addiction: A Complication of Modern Surgery?" Archives of Otolaryngology: Head and Neck Surgery, 112: 870-872 (1986); Cerny and Cerny, "Can Carrots Be Addictive? An Extraordinary Form of Drug Dependence," Br. J. Add. 87:1195 (1992).

desire is overpowering and leads to criminality and violence, if necessary, to satisfy the need for the drug.

In the 1988 Surgeon General's Report, the term "compulsive use" was expanded to include behaviors driven by "strong urges".[18] There is a world of difference between the irresistible need of the hard drug addict and a "strong urge" to engage in a pleasurable behavior or activity. People have strong urges to eat sweets, drink coffee and watch their favorite soap operas. It is misleading to label these types of "urges" as compulsions. Smokers are frequently in situations where they resist the urge to smoke. They are not in the throes of an overpowering desire to use and obtain cigarettes by any means. They do not remotely resemble cocaine addicts whose very real compulsion to take this highly intoxicating drug totally disrupts their lives, their families and their occupations.

Smokers are now constantly characterized as addicted and thus unable to quit. Common sense belies that conclusion. Since 1974, more than 40 million people have stopped smoking permanently without any outside intervention or assistance. As one ex-smoker has candidly acknowledged: "To quit, you have to decide you want to quit. Then you quit."[19]

[18] The full definition states: "Highly controlled or compulsive drug use indicates that drug seeking and drug-taking behavior is driven by strong, often irresistible urges". It provides no criteria for determining when a strong urge becomes "irresistible". In fact, no such criteria exist, as admitted by the American Psychiatric Association. "The line between an irresistible impulse and an impulse not resisted is no sharper than that between twilight and dusk. . . ." See "American Psychiatric Association Statement on The Insanity Defense", Am. J. Psychiatry, 140(6), 681-688, 1983.

[19] Leonard Larson, Scripp Howard News Service.

This is not to say that stopping smoking, or changing any well-liked, habitual behavior is easy. It takes effort and commitment. But, the process is not different from successfully losing several pounds and maintaining the weight loss or developing a regular exercise program. It is completely different from successfully recovering from hard drug addiction or alcoholism. The true addict must overcome severe physical withdrawal, rebuild every aspect of his life, learn new value systems, and approach life without being constantly intoxicated. None of these impediments is present in stopping smoking.

2. Psychoactive effect. Originally, the scientific community described the term "psychoactive" to include, as a necessary component, distortions or disruptions in cognitive and motor performance, i.e., intoxication. Those concepts were in effect for decades and were included in the 1964 Surgeon General's Report.[20] Smoking/nicotine, however, does not produce intoxication. To eliminate this inconvenient truth, the 1988 Surgeon General's Report redefined "psychoactive" to mean anything that gets to and produces effects in the brain. Based on this imprecise and revised definition, nicotine is psychoactive. So too is the caffeine in chocolate, coffee and soft drinks. Sugar, warm milk, cheeses, and many other everyday substances and common pleasant experiences (such as watching sporting events or listening to music) also produce psychoactive effects similar to those from smoking. They are quite unlike the profound effects caused by hard drugs and alcohol. It is the intoxication of hard drugs and alcohol that sets them apart and causes muddled thinking and loss of self control.

[20] Robinson, J.H. and Pritchard, W.S., "The Role of Nicotine in Tobacco Use." Psychopharmacology, 108, (4): 397-407, 1992.

Dr. Kessler testified that nicotine contained in cigarette smoke releases a certain chemical (dopamine) in the "pleasure centers" of the brain, resulting in similar effects as addicting drugs such as heroin and cocaine. Dr. Kessler failed to acknowledge that many different pleasurable and not so pleasurable experiences and activities also result in the release of dopamine in these "pleasure centers". Once again, the attempted analogy becomes meaningless when viewed objectively and without blinders. Dopamine release is one part of the neurochemical response to both pain and pleasure. It will occur if one receives an electric shock or slap in the face and also occurs in response to pleasant experiences of all kinds. Attempting to mystify a basic physical reaction and implying that it only occurs with addicting drugs is misleading at best.

3. Reinforcing behavior. Dr. Kessler's third criterion, reinforcing behavior, provides yet another example of the attempt to invest commonplace concepts with scientific mystique, combined with an erroneous implication that the condition only occurs with addicting drugs. Such is not the case. As presented in the 1988 Surgeon General's Report, reinforcing behavior merely refers to the fact that a pleasant experience will likely be repeated, whether it involves a chemical or activity.[21] Dr. Kessler cites two lines of evidence as support for his claims regarding reinforcement from nicotine:

1. That animals can be trained to self-administer nicotine; and
2. The experiments which claim that nicotine causes activation of "pleasure centers" in the brain involving dopamine.

[21] The report artificially attempts to separate reinforcement involving chemicals from those involving activities. In reality, it is the magnitude of the effect that is most important, not the source. Further, we reject the notion that the reinforcement, or pleasure, derived from cigarette smoking is solely the result of ingestion of nicotine.

Although it is true that animals will self-administer nicotine under certain very limited circumstances, this does not imply that the effects produced by or the motivation for ingesting nicotine are in any way similar to those of truly "addicting" drugs. Scientists at the Bowman Gray School of Medicine, in association with a Reynolds Tobacco scientist, recently published a peer-reviewed study demonstrating that nicotine and caffeine are very weak reinforcers when compared to cocaine and methylphenidate (Ritalin®).[22] Their findings were in line with the overall weight of the scientific evidence, which has consistently found caffeine and nicotine are both weak reinforcers.[23] Animals can be trained to self-administer a wide variety of substances. Animals have been trained to self-administer very painful electric shocks, and morphine addicted monkeys have been trained to self-administer opiate antagonists, precipitating very painful withdrawal symptoms. However, none of these self-administration behaviors proves the existence of an "addiction". Moreover, animals do not have to be extensively trained to self-administer cocaine or heroin. Once they start receiving either drug, they quickly become hooked and self-administer it to the exclusion of food and water and until death if not stopped.

4. Withdrawal symptoms. Although nicotine withdrawal was defined in 1987 by the American Psychiatric Association (DSM-III-R) as an element of tobacco dependence,

[22] Dworkin, et al., "Comparing the Reinforcing Effects of Nicotine, Caffeine, Methylphenidate and Cocaine." Medical Chemistry Research, Vol. 2:593-602 (1993).

[23] Griffiths, R.R., Brady, J.V., and Bigelow, G.E., "Predicting The Dependence Liability of Stimulant Drugs" in Thompson and Johanson Behavioral Pharmacology of Human Drug Dependence, NIDA Monograph 37, 1981, p. 92. This position has not changed. Griffiths, R., American Psychiatric Association Annual Meeting, San Francisco, CA, (1991).

the associated symptoms were identified in the 1964 Surgeon General's Report: restlessness, anxiety, trouble concentrating, and other "mild and variable symptoms".[24] That report stated that these symptoms were the same as those seen when any well-liked behavior was suddenly stopped. Nothing new has been established in this area. Caffeine withdrawal is much more well-established and well-defined, including the physical symptom of the "caffeine headache." Under Dr. Kessler's definition, caffeine and heroin should be treated equally.

Smoking cessation never involves any of the severe physical and behavioral disruptions involved in withdrawal from truly addicting drugs such as heroin, cocaine, and amphetamines. In fact, the symptoms of hard drug withdrawal normally require medical treatment. With many drugs (e.g. barbiturates and alcohol), the addict can die from withdrawal if not medically treated. An addict undergoing withdrawal from hard drugs is unable to think clearly or control his actions while in the throes of withdrawal. This is never the case with cigarette smokers who quit. They continue to attend to their responsibilities and lead normal lives. The symptoms reported by cigarette smokers when they stop are of the same kind and magnitude reported by dieters and people changing sleep patterns (e.g. changing from the first to third shift at work).[25]

[24] 1964 Surgeon General's Report, supra, at 352.

[25] It should be noted that DSM-III-R states that there is no evidence that, even at its most severe level, tobacco withdrawal prevents a person from successfully stopping. The same can not be said for barbiturates, alcohol or crack cocaine. Diagnostic and Statistical Manual of Mental Disorders (Third Edition - Revised) American Psychiatric Association, (1987), 151.

Cigarette smoking is more like drinking coffee and eating chocolate than like using cocaine, heroin, or any truly addicting hard drug. Cigarettes, however, are unpopular, which is why our critics strain so mightily to demonstrate that smoking is "addictive". The plain truth is that, under any objective scientific (or common sense) measure, cigarette smoking should not be considered "addictive".

Dr. Kessler and others support their assertions by repeating a deluge of facts that, in their judgment, prove their conclusions. Let us examine just a few of these "facts":

- First, Dr. Kessler quotes a 1993 Gallup Survey reporting that 75% of smokers say they are addicted. What Dr. Kessler does not report is that the same survey found that 69% of the same smokers said they "could quit if I wanted to." Moreover, this survey was conducted after the well-publicized 1988 Surgeon General's Report, which equated cigarette smoking with cocaine and heroin addiction. Does Dr. Kessler not believe that such publicity could affect responses to this survey?

- Dr. Kessler states that "By some estimates, as many as 74 to 90 percent are addicted." He relies on a paper by Hughes, et al. This paper also included the comment, "In addition, the fact that this definition [referring to DSM-III-R] classified 90% of the tobacco users in this study as dependent suggests that it is over inclusive and thus may lack diagnostic discriminability".

- Dr. Kessler makes repeated references to how certain percentages of people "may" or "might" possibly behave in certain circumstances. In one example, he discusses patients who continue to smoke after surgery or a coronary event. Some continue to smoke; most quit. Some also follow their doctor's advice and eat less fat, exercise regularly and lose weight. Some don't. The fact that human behaviors run a wide gamut when faced with similar situations tells us something about human behavior and little about smoking or nicotine.

- Dr. Kessler's "experts" tell him that most smokers reach for their first cigarette within 30 minutes of waking. He concludes that this fact is "a meaningful measure of addiction". By this measure most coffee drinkers should be considered addicts.

> Manufacturers of coffee makers have even developed machines which have coffee prepared by exact times to ensure that the coffee "addiction" can be satisfied immediately upon awakening.

It should be pointed out that Dr. Kessler's "definition" of addiction would classify most coffee, cola, and tea drinkers as caffeine addicts. Caffeine is psychoactive and the effects last longer than those of nicotine.[26] Many people experience a "strong urge" for a cup of coffee each morning. There is a well-established physical withdrawal syndrome for 2-3 cups a day coffee drinkers who suddenly stop drinking coffee. Is caffeine similar to cocaine and heroin because of this? Neil Benowitz, one of the editors of the 1988 Surgeon General's Report, admitted that caffeine meets their new definition of addiction:

> Many physicians have treated patients who continue to drink large quantities of caffeinated beverages in the face of information that caffeine is harmful to their health and advice to quit. Such behavior suggests that these people are addicted to caffeine. Addiction liability can be analyzed according to criteria recently presented by the United States Surgeon General. The three major criteria for addiction liability are psychoactivity, drug-reinforced behavior, and compulsive use. That caffeine is psychoactive and that some people consume caffeine compulsively is clear. That caffeine reinforces its consumption has recently been demonstrated in people, although reinforcement is highly dependent on the dose, with excess doses producing dysphoria. Minor criteria for addiction liability include the development of tolerance, physical dependence, and recurrent intense desire for the drug, all of which are characteristic of regular caffeine consumers. Thus, there is a group of coffee drinkers who appear to be addicted

[26] See Jaffe, J. and Kantzer, M., "Nicotine: Tobacco Use, Abuse and Dependence, Subst. Abuse, 0(0): 256, 1981. See also Sawyer et al., "Caffeine and Human Behavior: Arousal, Anxiety and Performance Effects, J. of Behav. Med., 5(4): 415, 1982. "Caffeine is, without question, the most commonly used psychoactive drug in the World." Jaffe, J.H., Comprehensive Textbook of Psychiatry, Chapter 13, Psychoactive Substance Use Disorders, 1(0), page 683, 1989.

> to caffeine, although the extent of caffeine addiction in the population is unknown.[27]

If the same "standards" are applied to caffeine, should the FDA also be considering (or should you suggest that it begin) regulating coffee and soft drinks as drugs?

One final point is important. Essentially every claim made about manipulating nicotine in cigarettes by Dr. Kessler can be made about alcohol in beer, wine and spirits. Spirits manufacturers constantly monitor the alcohol content of their products throughout the fermentation process to precisely control the level of alcohol. Beers and wines are offered to the public with a wide range of alcohol content. Alcohol is added to fortified wines. High alcohol malt liquors are also available to the public. While no one will dispute that alcohol can be a truly "addicting" substance under any definition, there is no move to regulate alcohol as a drug, and we do not believe there should be.

Why People Choose to Smoke

Dr. Kessler dismisses the issue of why people smoke by concluding, as the anti-smoking supporters he relies upon conclude, that smoking is an "addiction" and smokers would quit if they could break this "addiction". In the current climate of social disapproval and "political correctness", it is unpopular for smokers to honestly state that they smoke for pleasure and enjoyment. Yet for hundreds of years smoking has been accepted as a social custom, providing a pleasurable, enjoyable break from normal activities. Smokers enjoy the taste and other sensory aspects of smoking. A few moments with a cigarette can be a break

[27] Benowitz, N.L., "Clinical Pharmacology of Caffeine." Ann. Rev. Med., 41(0) 277-288, 1990.

during boring or intensive tasks, or a nice complement to a meal. All of these highly subjective reasons for smoking have found support in scientific publications.

Dr. Kessler pejoratively refers to "top tobacco industry officials" when referencing internationally respected Reynolds Tobacco scientists who have published widely in peer-reviewed scientific journals because they do not believe that tobacco is addictive. He then goes on to mischaracterize their data. In the journal article referenced by Dr. Kessler, Drs. Robinson and Pritchard summed up the evidence concerning addiction and tobacco use:

> We believe that Warburton (1990) has developed a balanced, functional theory of nicotine use that recognizes the beneficial psychological effects of nicotine. This "resource" or "psychological tool" hypothesis holds that people smoke cigarettes primarily for purposes of enjoyment, performance enhancement and/or anxiety reduction. This theory also passes the common sense test of why people smoke. They smoke, not because they are addicted to nicotine, but because they achieve some benefits from smoking, enjoy these benefits which are totally compatible with everyday tasks and stresses, and choose to continue to enjoy these benefits . . . .
>
> We believe the distinctions are clear and cannot be stated more clearly than what was said in the 1964 SGR [Surgeon General's Report]: "the practice [smoking] should be labeled habituation to distinguish it clearly from addiction, since the biological effects of tobacco, like coffee and other caffeine-containing beverages, . . . are not comparable to those produced by morphine, alcohol, barbiturates, and many other potent addicting drugs" (p. 350, emphasis in original). If we lose this common-sense perspective of the role of nicotine in tobacco use, those of us who enjoy the "lift" we receive from that first cup of coffee in the morning or that cola drink in the late afternoon may find that a few years from now a small group of researchers have equated our coffee/cola-drinking behavior to that of a hard-core crack or heroin addict.[38]

[38] Robinson and Pritchard, supra, at 405-6.

No scientific breakthrough has occurred since the 1964 Surgeon General's Report to warrant classifying cigarette smoking as "addictive". All of the essential facts describing the behavior have been well known for years. The only thing that has changed is the political climate surrounding cigarette smoking, and with it the ability of anti-smoking critics to develop a new definition of "addiction" solely to include cigarette smoking within it.

Conclusion

The facts are clear:

- Reynolds Tobacco does not add nicotine to its cigarettes.
- Reynolds Tobacco does not manipulate nicotine yields in its cigarettes in order to create, maintain, or satisfy "addiction".
- Cigarette smoking is not an "addiction" under common sense and honest comparison with truly "addicting" drugs.

Simply put, there is no factual basis or policy reason for the FDA to regulate cigarettes as drugs. The result of FDA regulation, moreover, would be a ban, or prohibition, of cigarettes. Dr. Kessler made this point clear in his recent statement before the Subcommittee. Members of this Subcommittee have stated that a ban or prohibition is not their intent; the American public resoundingly rejects the prohibition of cigarettes as well. We encourage a dialogue that will lead to progress rather than prohibition.

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RJR

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RESEARCH PLANNING MEMORANDUM

ON

THE NATURE OF THE TOBACCO BUSINESS AND THE CRUCIAL

ROLE OF NICOTINE THEREIN

CONFIDENTIAL

Exhibit 24 11
Date 5/29/97
A.W.R. & Assoc.

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PLAINTIFF'S EXHIBIT 5708
ALL-STATE LEGAL SUPPLY CO.

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In a sense, the tobacco industry may be thought of as being a specialized, highly ritualized and stylized segment of the pharmaceutical industry. Tobacco products, uniquely, contain and deliver nicotine, a potent drug with a variety of physiological effects. Related alkaloids, and probably other compounds, with desired physiological effects are also present in tobacco and/or its smoke. Nicotine is known to be a habit-forming alkaloid, hence the confirmed user of tobacco products is primarily seeking the physiological "satisfaction" derived from nicotine -- and perhaps other active compounds. His choice of product and pattern of usage are primarily determined by his individual nicotine dosage requirements and secondarily by a variety of other considerations including flavor and irritancy of the product, social patterns and needs, physical and manipulative gratifications, convenience, cost, health considerations and the like. Thus a tobacco product is, in essence, a vehicle for delivery of nicotine, designed to deliver the nicotine in a generally acceptable and attractive form. Our Industry is then based upon design, manufacture and sale of attractive dosage forms of nicotine, and our Company's position in our Industry is determined by our ability to produce dosage forms of nicotine which have more overall value, tangible or intangible, to the consumer than those of our competitors.

The habituated user of tobacco products is said to derive "satisfaction" from nicotine. Although much studied, the physiological actions of nicotine are still poorly understood and appear to be many and varied. For example, in different situations and at different dose levels, nicotine appears to act as a stimulant, depressant, tranquilizer, psychic energizer, appetite reducer, anti-fatigue agent, or energizer, to name but a few of the varied and often

contradictory effects attributed to it. Many of these same effects may be achieved with other physiologically active materials such as caffeine, alcohol, tranquilizers, sedatives, euphorics, and the like. Therefore, in addition to competing with products of the tobacco industry, our products may, in a sense, compete with a variety of other products with certain types of drug action. All of these products, tobacco and other, appear to have certain common attributes in that they are used largely to relieve, in one way or another, the fatigues and stresses which arise in the course of existence in a complex society.

Happily for the tobacco industry, nicotine is both habituating and unique in its variety of physiological actions, hence no other active material or combination of materials provides equivalent "satisfaction". Whether nicotine will, over the long term, maintain its unique position is subject to some reasonable doubt. With increased sophistication of knowledge in the biological and pharmaceutical areas, a superior or at least equivalent product or product mixture may emerge. For this reason, it would be a mistake to assume that the tobacco industry, as we now know it, is immortal or that no direct competition from organizations outside of the tobacco industry will ever occur. It is safe to assume, however, that nicotine will retain its unique position throughout the present ten year planning period, and probably for a much longer span of time.

If nicotine is the sine qua non of tobacco products and tobacco products are recognized as being attractive dosage forms of nicotine, then it is logical to design our products -- and where possible, our advertising -- around nicotine delivery rather than "tar" delivery or flavor. To do this we need to

develop new data on such things as the physiological effects of nicotine, the rate of absorption and elimination of nicotine delivered in different doses at different frequencies and by different routes, and ways of enhancing or diminishing nicotine effects and "satisfactions". In the absence of such data, we may survey the market and conclude that current cigarette products delivering about 1.3 mg. of nicotine appear to "satisfy" the typical smoker. This, somewhat crudely, establishes a target dosage level for design of new products. An accompanying Research Planning Proposal describes that approach in some detail. However, if we knew more about nicotine absorption, action, elimination, enhancement and the like, it should, in theory, be possible to more precisely specify, and deliver, the optimum amounts of nicotine activity in sophisticated products which would be more satisfying and desirable to the user. This area merits consideration and activity.

Before proceeding too far in the direction of design of dosage forms for nicotine, it may be well to consider another aspect of our business; that is, the factors which induce a pre-smoker or non-smoker to become a habituated smoker. Paradoxically, the things which keep a confirmed smoker habituated and "satisfied", i.e., nicotine and secondary physical and manipulative gratifications, are unknown and/or largely unexplained to the non-smoker. He does not start smoking to obtain undefined physiological gratifications or reliefs, and certainly he does not start to smoke to satisfy a non-existent craving for nicotine. Rather, he appears to start to smoke for purely psychological reasons -- to emulate a valued image, to conform, to experiment, to defy, to be daring, to have something to do with his hands, and the like. Only after experiencing smoking for some period of time do the physiological "satisfactions" and habituation become apparent and needed. Indeed, the first

smoking experiences are often unpleasant until a tolerance for nicotine has been developed. This leaves us, then, in the position of attempting to design and promote the same product to two different types of market with two different sets of motivations, needs and expectations. The same situation is encountered in some industries, but the problem is usually not as severe.

If what we have said about the habituated smoker is true, then products designed for him should emphasize nicotine, nicotine delivery efficiency, nicotine satisfaction, and the like. What we should really make and sell would be the proper dosage form of nicotine with as many other built-in attractions and gratifications as possible -- that is, an efficient nicotine delivery system with satisfactory flavor, mildness, convenience, cost, etc. On the other hand, if we are to attract the non-smoker or pre-smoker, there is nothing in this type of product that he would currently understand or desire. We have deliberately played down the role of nicotine, hence the non-smoker has little or no knowledge of what satisfactions it may offer him and no desire to try it. Instead, we somehow must convince him with wholly irrational reasons that he should try smoking, in the hope that he will for himself then discover the real "satisfactions" obtainable. And, of course, in the present advertising climate, our opportunities to talk to the pre-smoker are increasingly limited, and therefore, increasingly ineffective. Would it not be better, in the long run, to identify in our own minds and in the minds of our customers what we are really selling, i.e., nicotine satisfaction? This would enable us to speak directly of the virtues of our product to the confirmed smoker, and would educate the pre-smoker, perhaps indirectly but effectively, in what we have to offer and what it would be expected to do for him.

But again, the picture is not quite all that clear. Critics of tobacco products increasingly allege that smoking is dangerous to the health of the smoker. Part of this alleged danger is claimed to arise from ingestion of nicotine and part is claimed to arise from smoke components or smoke "tar". If, as proposed above, nicotine is the <u>sine qua non</u> of smoking, and if we meekly accept the allegations of our critics and move toward reduction or elimination of nicotine from our products, then we shall eventually liquidate our business. If we intend to remain in business and our business is the manufacture and sale of dosage forms of nicotine, then at some point we must make a stand. We should know more, rather than less, than our critics about the physiological effects of nicotine, and we should in all ways scientifically validate and speak to the beneficial effects and "satisfactions" derived from use of nicotine. Essentially all commercial drugs give rise to some undesirable side effects, but we continue to use them with great benefit to humanity because of their overriding beneficial effects. Might we not take a leaf from that book in our approach to nicotine? Unless we do, our long-term prospects become unattractive.

Our critics have lumped "tar" and nicotine together in their allegations about health hazards, perhaps because "tar" and nicotine are generated together in varying proportions when tobacco is smoked. An accompanying Research Planning Memorandum suggests an approach to reducing the amount of "tar" in cigarette smoke per unit of nicotine. That is probably the most realistic approach in today's market for conventional cigarette products. However, another more futuristic approach is possible which goes more directly to the fundamentals of the alleged problem.

If our business is fundamentally that of supplying nicotine in useful dosage form, why is it really necessary that allegedly harmful "tar" accompany that nicotine? There should be some simpler, "cleaner", more efficient and direct way to provide the desired nicotine dosage than the present system involving combustion of tobacco or even chewing of tobacco. A conventional 1000 mg. tobacco rod containing about 20 mg. of nicotine is smoked to produce only about 1.3 mg of smoke nicotine, accompanied by about 20 mg. of "tar" and 20 mg. of gas phase matter; and a ~~substantial~~ part of the 1.3 mg of smoke nicotine is lost to the smoker via exhaled smoke -- surely an inefficient nicotine delivery system. It should be possible to obtain pure nicotine by synthesis or from high-nicotine tobacco. It should then be possible, using modifications of techniques developed by the pharmaceutical and other industries, to deliver that nicotine to the user in efficient, effective, attractive dosage form, accompanied by no "tar", gas phase, or other allegedly harmful substances. The dosage form could incorporate various flavorants, enhancers, and like desirable additives, and would be designed to deliver the minimum effective amount of nicotine at the desired release-rate to supply the "satisfaction" desired by the user. Such a product would maximize the benefits derived from nicotine, minimize allegedly undesirable over-dosage side effects from nicotine, and eliminate exposure to other materials alleged to be harmful to the user. For the long term, we should be working toward development of such products -- if we do not inevitably someone else will, and there are strong indications that others are already moving in this direction.

In the present real situation, where nothing has been done to counteract the adverse allegations about nicotine and where conventional products delivering adequate amounts of nicotine dominate the marketplace, no abrupt change in our posture or strategy would be appropriate or reasonable. The approaches advocated above are aimed at stopping and eventually reversing a trend that may in the long term put us out of business, and are intended to lay a framework of philosophy around which research efforts may now begin. Hopefully, some day we will rejoice rather than despair when a new crop of tobacco shows an unusually high content of nicotine, our primary product. Hopefully, with time we will be able to develop sophisticated and improved minimum dosage forms for nicotine which will be more satisfying to the user and free of alleged health hazards. And hopefully, by that time, we will have been able to establish and use information showing that use of nicotine fills real, demonstrable human needs, the beneficial effects overriding the allegedly harmful side effects.

INDICATED RESEARCH DEPARTMENT ACTIVITIES AND APPROACHES:

If the above is a valid line of reasoning, then our long-term future courses of action should be as follow:

1. Recognize the key role of nicotine in consumer satisfaction, and design and promote our products with this in mind.
2. More precisely define the minimum amount of nicotine required for "satisfaction" in terms of dose levels, dose frequency, dosage form, and the like. This would involve biological and other experiments.
3. Sponsor in-depth studies of the physiological, psychological and other effects of nicotine, aimed at demonstrating the beneficial effects of nicotine and at disproving allegations that nicotine produces major adverse effects.

4. Study, design and evaluate new or improved systems for delivery of nicotine which will provide the minimum satisfying amount of nicotine in attractive form, free of allegedly harmful combustion products.
5. Study means for enhancing nicotine satisfaction via synergists, alteration of pH, or other means, to minimize dose level and maximize desired effects.
6. Monitor developments in materials and products which may compete with nicotine products or which might be combined with nicotine-products to provide added advantages or satisfactions.
7. Monitor work by others which might be aimed at improved nicotine delivery systems of the type proposed here.
8. Search for and evaluate other physiologically active components of tobacco or its smoke which may provide desired effects to the smoker.

Claude E. Teague, Jr.
April 14, 1972

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AMMONIA

Ammonia is used by RJRT in the following tobacco processing operations.

(1) Denicotinization of burley tobacco

(2) Ammoniation of reconstituted tobacco

Denicotinization of Burley Tobacco

Denicotinization of some of our burley tobacco gives us greater flexibility in the type of tobacco we can use in our products to meet the constantly changing demands by consumers for cigarette products with different tar and nicotine levels. This process also permits us to partially or completely compensate for the variability in the nicotine content of tobacco from year to year, market to market, etc. when desired.

In the RJRT denicotinization process, burley tobacco is first treated with gaseous ammonia, and then contacted with steam to remove nicotine and excess ammonia. Since the major portion of the nicotine in the tobacco is present as nicotine salts (citate, oxalate, malate), the major portion of the residual ammonia is present in the form of the ammonium salts of the acids.

Denicotinization produces the following changes in the chemical composition of burley tobacco and smoke: (1) decreased nicotine content of the tobacco; (2) decreased levels of nicotine, related alkaloids, pyrazines and pyridines in the smoke; (3) increased ammonia content of the tobacco; and (4) increased level of ammonia in the smoke.

The magnitude of some of the chemical changes that occur in burley tobacco and smoke are shown in Table I. These data were taken from a report by C. R. Green et. al., RDR, 1976, No. 3.

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TABLE I

EFFECT OF DN PROCESSING ON BURLEY[a] SMOKE AND TOBACCO COMPOSITION

Analysis	L8120A	L8120B	% Difference	L8769A	L8769B	% Difference[b]
Smoke[c]						
TPM, mg	35.0	33.0	ND	37.4	31.9	-15
TPM water, mg	4.3	3.9	ND	4.8	3.7	-23
Nicotine, mg	4.17	1.80	-57	5.22	1.70	-67
FTC "tar", mg	26.5	27.2	ND	27.4	26.5	ND
Puffs	8.9	8.9	ND	9.1	8.9	ND
pH, Average Min.	7.03	7.08		7.03	6.66	
Average Max.	7.78	8.41		7.89	8.24	
Carbon monoxide, mg	15.4	17.6	14	19.0	19.4	ND
Formaldehyde, g	49	50	ND	106	103	ND
Acetaldehyde, g	955	895	ND	965	930	ND
Acrolein, g	81	69	-15	93	82	ND
Ammonia, g	87	178	105	128	261	104
Hydrogen cyanide, g	257	279	ND	314	322	ND
Nitrogen oxides[e], g	712	752	27	540	470	-13
Isoprene, g	835	81	-15	103	113	ND
Benzo[a]-pyrene, ng	11.2	10.7	ND	-	-	-
Weight, g	1.111	1.074				
PD, Inches Water	2.80	2.62				
Sugars, %	1.7	1.4	-17			
Nicotine, %	3.22	1.24	-61			
Ammonia, %	0.70	0.82	17			

[a]Control Burley = L8120A or L8769A Test Burley = L8120B or L8769B

[b]% Difference = 100 (A-B)/B where A = DN burley value, B = Control burley value

[c]Value per cigarette

[d]ND = No difference; values fall within + 10%

[e]Nitrogen oxides are expressed as NO_2

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RJRT is currently using 0-12 percent denicotinized burley tobacco, based on the total blend, in all brands except the NOW Family. The NOW brands contain 18-24 percent denicotinized burley tobacco based on the total blend.

Ammoniation of Reconstituted Tobacco

Studies on the ammoniation of reconstituted tobacco were started in 1973 as a result of R&D studies carried out during the 1950's and early 1970. During the 1950's, Dr. C. E. Teague, Jr. investigated the ammoniation of tobacco and tobacco stems and reported dramatic improvements in the smoking qualities of ammoniated tobacco stems. Smoke harshness and irritation~~s~~ were reduced and taste properties were improved.

In the early 1970's, a major R&D program was initiated to investigate the physical chemistry of tobacco and tobacco smoke in an attempt to gain a better understanding of the factors affecting smoke harshness, irritation and strength~~s~~. These studies led to the following observations and conclusions.

(1) The pH of cigarette smoke is important to smoke quality and can be used as a measure of the physiological strength of smoke.

(2) Ammonia in smoke is one of the major pH controlling components. Others include nicotine, amines, organic acids and carbon dioxide.

trace amounts

(3) Ammonia occurs naturally in tobacco ranging from almost none in flue-cured tobacco to over 1 percent in high quality cigar tobacco.

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(4) Philip Morris introduced the use of added ammonia in their cigarette products in 1965. They use diammonium hydrogen phosphate in their reconstituted tobacco process to liberate ammonimum pectinate prior to casting a reconstituted tobacco sheet (RDM, 1972, No. 10).

(5) Philip Morris brands, especially Marlboro, began growing in sales very rapidly after the introduction of added ammonium.

(6) Correlation studies relating increased smoke pH to sales trends showed a very strong positive correlation (RDM, 1973, No.17).

(7) Studies of the effect of ammonia in smoke composition showed a reduction in aldehydes, especially formaldehyde, and an increase in the levels of pyridines, pyrazines, and minor alkaloids. Smoking panel results showed a decrease in smoke irritation and harshness and an increase in physiological satisfaction with increasing ammonia content.

Based on the above observations, it was decided to investigate the use of ammoniated reconstituted tobacco (G7A) as a means of increasing the smoke pH of RJRT cigarette products. NFO tests indicate that smokers prefer products containing G7A over products containing only G7 ~~[illegible]~~ (untreated reconstituted tobacco). Since the introduction in CAMEL Filter in 1975, G7A has been tested and/or introduced in nineteen additional brands at levels slightly greater than ~~ranging to~~ 27% ~~plus~~.

RJR analytical data show that the current CAMEL Filter, which contains both denicotinized tobacco (7.6 percent based on total blend) and G7A (27.64 percent based on total blend), delivers approximately 36 μg of ammonia per cigarette in the mainstream smoke. A two-pack-a-day smoker will be exposed to approximately 1440 μg of ammonia.

BIOLOGICAL DATA ON AMMONIA

Introduction:

Ammonia is a normal body constituent which participates in many of the body's catabolic and metabolic processes. Excess amounts of ammonia produced in the body are converted to and excreted as urea in the urine.

Ammonia or its salts are normal components of ~~our~~ many constituents of food supply. Also a number of ammonia containing compounds are considered GRAS when used as miscellaneous and/or general purpose food additives. These include ammonium hydroxide, ammonium bicarbonate, ammonium carbonate, ammonium saccharin, ammonium sulfate and ammonium phosphate. Other specific applications permit the use of ammonium caseinate, ammonium chloride, ammonium isovalerate, ammonium persulfate, ammonium sulfide, ammonium sulfite, etc. IN FOOD PRODUCTS

Clearly, the use of ammonia in the processes described in this paper are similar to many of the applications commonly used in the food industry. Hence there would be little reason to expect any undesirable effects. ¶ Although the total NH_3 in tobacco smoke can be determined, the actual form of the NH_3 is probably as the salts of carbonic acid, malic acid, isovaleric acid, and other organic acids. Ammonia salts of acids with the exception of the salts of strong acid such as hydrochoric and sulfuric acid are usually less irritating and less toxic than free ammonia. Hence, if we compare the level of total ammonia in cigarette smoke with the known biological effects of ammonia we are no doubt overestimating any effect.

Acute Toxicity[1]:

The acute oral toxicity (LD50) of ammonia in rats if 350 mg/kg. body weight. The maximum exposure of a two pack a day smoker is estimated to be 1.44 mg of NH_3 per day. A 60 kg. person would therefore be exposed to 0.024 mg/kg body weight. Therefore the LD50 is more than 14000 times the ammonia exposure of the two pack a day smoker.

Inhalation Toxicity

Ammonia is a respiratory irritant and inhalation in high concentrations may cause edema of the respiratory tract, fit of glottis and suffocation. The lethal concentration in cats (LC50) was determined to be 10000 ppm for one hour.

Comparison of Smoker Exposure to Threshold Limit Value Exposure

Because of the extensive use of ammonia in commercial processes such as in the manufacture of fertilizer nitric acid, hydrazine hydrate, nitriding of steel, etc. the determination of safe exposure levels for workers in industry has been thoroughly investigated. As a result Threshold Limit Values for exposure have been set. It is of interest to compare the level of exposure permitted ~~in industry~~ for ammonia the work place to ~~that~~ the maximum potential ammonia exposure a smoker receives when smoking cigarettes. This is shown below.

According to 1981 ACGIH recommendations, the Threshold Limit Value (TLV) for ammonia is 18 mg/m^3 of air. It is estimated that the average person inhales 10 m^3 air in an eight-hour period (International Commission on Radiology Protection: Report of Task Group on Reference Man, Pergamon Press). During an eight-hour work day, a person working in an atmosphere containing 18 mg of ammonia per cubic meter of air would inhale 180 mg of ammonia. This is 125 times the estimated daily dose for a two-pack-a-day CAMEL Filter smoker.

These two types of exposure may not be comparable because the occupational exposure is spread over an eight-hour day, and the cigarette exposure occurs during irregularly spaced intervals throughout the day. According to ACGIH regulations, a short-term exposure limit (less than 15 minutes) to ammonia at 27 mg/m^3 is permissible. A person working in an atmosphere containing 27 mg of ammonia/~~per cubic~~ meter^3 of air would inhale 8.4 mg of ammonia in 15 minutes. This is over 200 times the amount of ammonia a smoker would inhale if he or she smoked one CAMEL Filter cigarette very 15 minutes.

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Federal Trade Commission

TAR, NICOTINE, AND CARBON MONOXIDE
OF THE SMOKE OF 1107 VARIETIES
OF DOMESTIC CIGARETTES

[illegible]
Exhibit [illegible]
Date 5/14/97
A.W.R. & Assoc.

1995

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BRAND NAME	DESCRIPTION	TAR	NIC	CO
RIVIERA	100 F SP FF MEN	17	1.2	16
RIVIERA	100 F SP LT MEN	11	.9	11
RIVIERA	KING F HP FF MEN	17	1.1	15
RIVIERA	KING F SP FF MEN	15	1.1	13
RIVIERA	KING F SP LT MEN	11	.9	11
ROTHMANS*	KING F HP	16	1.2	18
ROTHMANS*	KING F HP	16	1.2	NA
ROTHMANS*	KING F HP SPECIAL	12	1	12
ROTHMANS*	KING F HP SPECIAL	13	1.1	NA
ROTHMANS*	KING F HP EXTRA-LT	10	1.1	NA
SALEM	100 F HP LT MEN	11	.9	11
SALEM	100 F HP SLIM MEN	9	.7	8
SALEM	100 F SP MEN	17	1.2	18
SALEM	100 F SP LT MEN	9	.7	11
SALEM	100 F SP ULTRA-LT MEN	5	.5	8
SALEM	KING F SP MEN	18	1.3	18
SALEM	KING F SP LT MEN	10	.8	12
SALEM	KING F SP ULTRA-LT MEN	5	.4	7
SALEM GOLD	KING F HP MEN	18	1.4	18
SALEM GOLD	KING F HP LT MEN	13	1	15
SALEM*	100 F HP SLIM MEN ULTRA	5	.4	8
SALEM*	100 F HP SLIM-LT MEN	9	.7	8
SALEM*	100 F SP MEN	15	1.1	17
SALEM*	100 F SP LT MEN	8	.7	10
SARATOGA	120 F HP	14	1.1	13
SARATOGA	120 F HP MEN	14	1.1	13
SATIN	100 F SP	12	1	13
SATIN	100 F SP MEN	12	1	13
SAVANNAH	100 F HP SLIM-LT SLIM	8	.7	8
SAVANNAH	100 F HP SLIM-LT MEN	7	.6	7
SAVVY*	100 F SP LT	12	1.1	13
SAVVY*	100 F SP LT MEN	12	1.1	13
SAVVY*	100 F SP ULTRA-LT	6	.7	5
SCOTCH BUY*	100 F SP FF	14	.9	18
SCOTCH BUY*	100 F SP LT	8	.7	11
SCOTCH BUY*	100 F SP LT MEN	9	.7	12
SCOTCH BUY*	100 F SP ULTRA-LT	5	.4	7
SCOTCH BUY*	KING F SP FF	14	.9	16
SCOTCH BUY*	KING F SP LT	9	.6	12
SCOTCH BUY*	KING F SP LT MEN	9	.7	13
SCOTCH BUY*	KING F SP ULTRA-LT	5	.4	6
SEBRING*	100 F SP FF	14	.9	18
SEBRING*	100 F SP FF MEN	17	1	18
SEBRING*	100 F SP LT	8	.7	11
SEBRING*	100 F SP LT MEN	9	.7	12
SEBRING*	100 F SP ULTRA-LT	5	.4	7
SEBRING*	KING F SP FF	14	.9	16
SEBRING*	KING F SP FF MEN	14	.9	16
SEBRING*	KING F SP LT	9	.6	12
SEBRING*	KING F SP LT MEN	9	.7	13
SEBRING*	KING F SP ULTRA-LT	5	.4	6
SEBRING*	KING NF SP	20	1.1	15

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BRAND NAME	DESCRIPTION	TAR	NIC	CO
VALUE TIME*	100 F SP FF MEN	17	1	18
VALUE TIME*	100 F SP LT	8	.7	11
VALUE TIME*	100 F SP LT MEN	9	.7	12
VALUE TIME*	100 F SP ULTRA	5	.4	7
VALUE TIME*	KING F SP FF	14	.9	16
VALUE TIME*	KING F SP FF MEN	14	.9	16
VALUE TIME*	KING F SP LT	9	.6	12
VALUE TIME*	KING F SP LT MEN	9	.7	13
VALUE TIME*	KING F SP ULTRA	5	.4	6
VALUE TIME*	KING NF SP	20	1.1	15
VANTAGE	100 F HP ULTRA-LT	5	.5	6
VANTAGE	100 F SP	8	.6	8
VANTAGE	100 F SP MEN	8	.6	10
VANTAGE	100 F SP ULTRA-LT	5	.4	7
VANTAGE	KING F HP ULTRA-LT	5	.5	6
VANTAGE	KING F SP	8	.6	8
VANTAGE	KING F SP MEN	8	.6	9
VANTAGE	KING F SP ULTRA-LT	5	.5	7
VICEROY	100 F HP	17	1.2	14
VICEROY	100 F HP LT	12	.9	14
VICEROY	100 F SP	17	1.2	14
VICEROY	100 F SP LT	12	.9	14
VICEROY	100 F SP ULTRA-LT	5	.5	6
VICEROY	KING F HP	16	1.1	14
VICEROY	KING F HP LT	11	.9	12
VICEROY	KING F SP	16	1.1	14
VICEROY	KING F SP LT	11	.9	12
VICEROY	KING F SP ULTRA-LT	6	.5	6
VIRGINIA SLIMS	100 F HP SUPER-SLIM	6	.5	6
VIRGINIA SLIMS	100 F HP MEN SUPER-SLIM	6	.5	5
VIRGINIA SLIMS	100 F HP LT SLIM	8	.7	8
VIRGINIA SLIMS	100 F HP LT MEN SLIM	8	.6	8
VIRGINIA SLIMS	100 F HP ULTRA-LT SLIM	6	.5	6
VIRGINIA SLIMS	100 F HP ULTRA-LT MEN SL	6	.5	6
VIRGINIA SLIMS	100 F SP SLIM	14	1.1	12
VIRGINIA SLIMS	100 F SP MEN SLIM	15	1.1	12
VIRGINIA SLIMS	120 F HP LT SLIM	4	1	13
VIRGINIA SLIMS	120 F HP LT MEN SLIM	14	1.1	13
VISTA*	KING F HP LT GEN	11	.7	NA
WINSTON	100 F HP LT	9	.7	10
WINSTON	100 F HP ULTRA-LT	6	.5	8
WINSTON	100 F SP	17	1.1	17
WINSTON	100 F SP LT	10	.7	13
WINSTON	100 F SP ULTRA-LT	4	.4	6
WINSTON	KING F HP	18	1.3	17
WINSTON	KING F HP LT	10	.7	11
WINSTON	KING F HP ULTRA-LT	5	.4	7
WINSTON	KING F SP	17	1.4	14
WINSTON	KING F SP LT	10	.7	11
WINSTON	KING F SP ULTRA-LT	6	.6	7
WINSTON SELECT*	100 F HP LT	11	.9	13
WINSTON SELECT*	100 F HP SLIM-LT	10	.8	9

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R.J.Reynolds Tobacco Compan
Winston-Salem NC 27102

RJR

January 11, 1990

Principal
Willow Ridge School
480 Willow Ridge Drive
Amherst, NY 14150

Dear Sir or Madam:

A number of your fifth grade students have written R.J. Reynolds Tobacco Company commenting that they do not feel our company should allow the use of our brand names on children's toys and candy cigarettes.

As information, R.J. Reynolds Tobacco Company's policy is not to allow our brand names to be used on toys or candy cigarettes and any current use of our brand names in this fashion is not sanctioned by our company.

Some of the students also commented about the controversies surrounding cigarette smoking. The tobacco industry considers smoking to be a custom for those adults who derive pleasure from it. We believe that whether to smoke or not is a decision that should be freely made by individuals who have reached the age of mature judgment. Accordingly, our advertising is directed to adult smokers and not younger people.

The tobacco industry is also concerned about the charges being made that smoking is responsible for so many serious diseases. Long before the present criticism began, the tobacco industry, in a sincere attempt to determine what harmful effects, if any, smoking might have on human health, established The Council for Tobacco Research--USA. The industry has also supported research grants directed by the American Medical Association. Over the years the tobacco industry has given in excess of $162 million to independent research on the controversies surrounding smoking -- more than all the voluntary health associations combined.

Despite all the research going on, the simple and unfortunate fact is that scientists do not know the cause or causes of the chronic diseases reported to be associated with smoking. The

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R.J. Reynolds Tobacco USA
Winston-Salem, N.C 27102

Principal
Page Two
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answers to the many unanswered controversies surrounding smoking and the fundamental causes of the diseases often statistically associated with smoking -- we believe can only be determined through much more scientific research. Our company intends, therefore, to continue to support such research in a continuing search for answers.

We would appreciate your passing this information along to your students. You may also be interested in the enclosed publications presenting the position of our company and the tobacco industry on the issue of youth smoking.

Sincerely,

Jo F. Spach

(Mrs.) Jo F. Spach
Manager, Public Information
Public Relations Department

JFS/jmd

Enclosures

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https://www.industrydocuments.ucsf.edu/docs/tggl0001

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BRITISH MEDICAL JOURNAL
LONDON SATURDAY FEBRUARY 7 1959

LABORATORY CONTRIBUTIONS TO THE TOBACCO-CANCER PROBLEM*

BY
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The sum total of evidence linking smoking to cancer of the respiratory tract is based upon different types of evidence: presumptive, epidemiological, pathological, animal, and chemical. All of the evidence so far established demonstrates smoking to be a carcinogenic factor. It is now our task to bring the problem posed by this association to a successful solution. The present report represents an evaluation of the contributions that laboratory research is making in this field.

The importance of laboratory work is not to prove that smoking is a cause of cancer in man. Such proof can only come from human epidemiological investigation. Laboratory research can, however, contribute to, and give a logical explanation for, the human findings. Just as an animal experiment cannot disprove that a given factor causes cancer in man because of possible species differences, so, by itself, an experiment cannot prove a given agent to be carcinogenic to man. It is primarily as a corollary to the human findings that the animal experiment has its significance. The basic tasks of laboratory research, which are of a biological and chemical nature, are to identify the specific agents in a given product that produces cancer and to devise ways and means whereby such agents can be reduced or removed. In so doing, we can only assume that the agents responsible for the activity in animals are also responsible for the human activity. In view of the many similarities established for tumour growth in animals and man, such an assumption, though it cannot be proved, stands on a firm foundation.

Most cancer researchers would surely agree that once a carcinogen has been identified in a given material suspected to be active for man and proved to be active for animal tissue, particularly when this is demonstrated for several species of animals, such an agent should, if at all possible, be reduced or eliminated from man's environment. It is along these lines that laboratory research, as it applies to the tobacco-cancer problem, has its greatest significance. It is now our purpose to review the methods followed in respect to this work and the results already achieved.

Methods of Study

Since the primary purpose of the biological study is to establish the activity of the agents suspected to be carcinogenic, the test site is perhaps less important than is generally considered. In choosing the test site, one must be sure not only to use a site which is not too sensitive to tumour formation, but also to avoid one in which tumours cannot be produced even with very potent carcinogens. In general, it would be advantageous to use the type of tissue similar to the one involved in man. In view of these considerations, the subcutaneous tissue of mice would be a less useful site because it does not yield epithelial tumours and also because it has been shown to be quite sensitive to a large variety of substances. On the other hand, the lungs of mice would not represent a good test organ, since, even upon inhaling high doses of potent polynuclear hydrocarbons,[33] it has been difficult to produce lesions in the bronchus of mice. The skin, on the other hand, is a satisfactory site not only because of ease of application, but also because it represents a type of tissue similar to the epithelial tissue of the respiratory tract.

An important factor when testing a product to which man is exposed is to test this product under a condition similar to that under which man is exposed. Thus we should smoke tobacco in a manner simulating human smoking habits, and should not distil the tobacco smoke in a closed container. Another important principle is that, when testing a substance suspected to be only weakly carcinogenic, the substance should be applied in maximum concentration over a maximum period of time. With these considerations on methodology we shall review the actual experiments already completed.

BIOLOGICAL DATA

Lung Studies

A number of experiments have been conducted exposing mice to cigarette smoke. As could be expected from similar experiments with pure carcinogens, it is most difficult to produce bronchiogenic lesions in this manner. The method is particularly difficult with tobacco smoke because if the concentration of the smoke is too high animal mortality is too great. Campbell, and later Essenberg, have succeeded in producing pulmonary adenomas in susceptible mice by exposing the animals to varying concentrations of cigarette smoke.[7, 14] Lorenz obtained negative results.[31] In a more recent and detailed study, the Leuchtenbergers found that there is an increase in hyperplasia, metaplasia, dysplasia, and carcinoma *in situ* when mice are exposed to cigarette smoke for a relatively short period of time.[31] These experiments are of interest because they show

*Presented before the Seventh International Cancer Congress in London, July 11, 1958.

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the same types of early bronchial changes as demonstrated by Auerbach and others[1,13,33] in human lungs.[34] Using a more direct approach, Rockey applied condensed cigarette smoke to the trachea of dogs for about 11 months, noting severe metaplasia of the epithelium.[40] Blacklock, injecting tobacco smoke condensate together with tubercle bacilli into the hilum of rats, was able to produce two carcinomas in the eight rats treated in this way.[4]

Though inhalation studies, therefore, have so far not produced any actual bronchiogenic carcinomas in the experimental animal, a result which could not be expected because of the toxicity of high doses of tobacco smoke and in view of the fact that this has been difficult even with high concentrations of polycyclics, the available evidence has nevertheless indicated an abnormal reaction of the pulmonary and bronchial tissue to tobacco smoke and in one instance the production of carcinoma in this tissue when the smoke condensate was directly applied.

Skin Studies

There are surprisingly few experiments dealing with the production of skin cancer in animals upon application of tobacco smoke condensate in view of the attention given to the problem. In fact, until 1953 no study had been done with condensed tobacco smoke. At that time we published our first report showing the production of 44% cancers and 59% papillomas among CAF_1 mice which had been painted with a 50% tar-acetone solution three times a week.[45] In 1955 we reported[47] the production of cancers in two additional strains of mice, Swiss and C_{57}. Since this time we have reported positive results on yet another mouse strain.[48] In the meantime, Hammer and Woodhouse, as well as Passey, reported their inability to produce skin cancer in mice with tobacco tar.[21,38] However, as will be shown subsequently, the negative results are not necessarily due to differences in British and American tobaccos but rather to the fact that the tar was applied at a subthreshold level. The fact that tobacco tar is carcinogenic to mouse skin has since been confirmed by Sugiura, by Bock, by Orris, and by Engelbreth-Holm.[6,15,35,44] These studies leave no doubt that tobacco smoke condensate is carcinogenic to mouse epidermis. In more recent experiments we demonstrated that carcinogenic activity is also present in cigar and pipe smoke.[14] In fact, we found a slightly greater activity in cigar and pipe smoke than in cigarette smoke.

Carcinomas have been produced not only in mice but also in rabbits. Roffo published a whole series of articles on the production of cancer in rabbit ears with a tobacco smoke distillate.[41] However, it could be argued that this distillate represented a variance from the tobacco smoke condensate. We recently reported the production of carcinoma in rabbit ears after applying cigarette smoke condensate over a period of six years five times a week, 100 mg. per painting, in a 50% tar-acetone solution: 100% of the rabbits developed papillomas and 12.5% of 48 rabbits developed histologically proved cancers. Two of these cancers showed widespread metastases.[50]

In summary, biological experiments to date have proved that tobacco smoke condensate is carcinogenic to at least two species of animals and several strains of mice.

Before the chemist could proceed to identify the active materials, biological study had to be conducted to determine the particular components of the total tar in which the majority of the activity is located. In a large-scale study, summarized in Fig. 1, we have shown

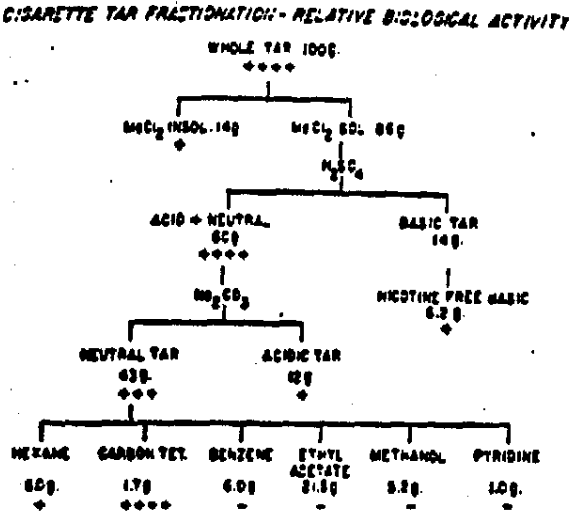

FIG. 1.—The plus sign indicates relative values of carcinogenic activity.

that the majority of the active fractions of tobacco smoke condensate are in the fraction which is eluted with carbon tetrachloride from the neutral tar.[49] This fraction, representing only 1.7% of the total tar, produces 100% cancer in animals when applied in 10% concentration. We did observe some activity in other fractions. However, it cannot be said whether this is a result of independent carcinogenic substances or whether it is the consequence of unsatisfactory chemical separation. Present data suggest that in the basic portion of the tar, where polynuclear substances are not thought to remain, there are at least cocarcinogenic elements.[49] This is believed to be the case not only because of the high hyperplastic reaction obtained with this material, but also because it increased the tumour yield when added to the neutral tar. However, we conclude at this time that the major carcinogens are in the carbon tetrachloride fraction of the neutral tar.

Chemical Data

The chemical studies have been directed toward identifying the agents in tobacco suspected to give rise to the carcinogenic activity of the total tar. The first suspicion obviously falls upon the higher aromatic polycyclics, since it is a well-established principle that the burning of any organic matter will give rise to these substances.[3,19] A large number of investigators have now identified 3:4-benzpyrene in tobacco smoke condensate, ranging up to 2 µg. per 100 cigarettes.[8,9,11,...] It is generally realized, of course, that this amount of benzpyrene is not sufficient to account by itself for the carcinogenic activity of the total tar. We have also reported the identification of 1:2:5:6-dibenzanthracene in cigarette smoke condensate again, though in minute amounts.[31] Tentative spectrographic identification has also indicated the presence of additional carcinogens such as 1:2-benzanthracene,[...] 1:2-benzpyrene,[...] 1:12-benzperylene,[...]

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chrysene,[21 24] 3:4:9:10-dibenzpyrene,[27] and 3:4:8:9-dibenzpyrene.[23 24] The last-named has also been tested by Buu-Hoi, but has relatively little biological activity for the skin.[24] Recently, Hoffmann, and also Van Duuren, have identified 3:4-benzfluoranthene, which we have proved to be carcinogenic to mouse skin.[23 21] Additional higher aromatic polycyclics identified but not yet tested for carcinogenic activity include benz(mno)-fluoranthene, 10:11-benzfluoranthene, and 11:12-benz-fluoranthene.[21 24]

Chemical work done at present in our laboratory is directed toward determining additional polycyclics in the various tobacco fractions found to be carcinogenic. In Table I, as most recently completed by Dr. Hoffmann,

TABLE I

Polycyclic Hydrocarbons	p.p.m. Fraction B	p.p.m. Fraction C
3:4-Benzpyrene	$0.57 \cdot 10^{3}$	$1.14 \cdot 10^{4}$
1:2:5:6-Dibenzanthracene	$0.24 \cdot 10^{3}$	$0.01 \cdot 10^{4}$
3:4-Benzfluoranthene	$0.055 \cdot 10^{4}$	$0.73 \cdot 10^{4}$
10:11-	$0.18 \cdot 10^{3}$	$0.08 \cdot 10^{4}$
1:2-Benzpyrene	$0.055 \cdot 10^{3}$	+
1:12-Benzperylene	$0.06 \cdot 10^{4}$	$0.99 \cdot 10^{3}$
1:2-Benzanthracene	+	–
Chrysene	$1.1 \cdot 10^{3}$	+
Alkylchrysene	$0.55 \cdot 10^{3}$	+
Fluoranthene	$0.93 \cdot 10^{4}$	–
Alkylfluoranthene	+	–
Pyrene	$4.0 \cdot 10^{3}$	–
Alkylpyrene	$1.6 \cdot 10^{3}$	–
Perylene	$0.03 \cdot 10^{2}$	–
11:12-Benzfluoranthene	$0.1 \cdot 10^{3}$	–
Benz(mno)fluoranthene	+	+
2:3-Benzfluorene	–	$0.1 \cdot 10^{4}$
Anthracene	+	–
Phenanthrene	+	–

Fraction B is the carbon tetrachloride eluate of the neutral tar (see Fig. 1). Fraction C is biologically the most active fraction of the 880° C. pyrolysate of a hot hexane extract of cigarette tobacco.

we show the identification of higher aromatics present in the carbon tetrachloride fraction of the neutral tar. Even though at present we may still not have identified all of the polycyclics responsible for the total activity of this fraction, the activity of this fraction is largely due to polycyclics. There obviously remain other polycyclics still to be identified, a project which may be of greater academic than practical importance, since it may be assumed that polycyclics are produced in the same manner. These tables also show the identification of polycyclics in Fraction C, representing one of the ten subfractions of the 880° C. pyrolysate of hexane extracted tobacco which, in 0.01% concentration, proved to be biologically active.[24] It is of interest that, even though a whole range of polycyclics was identified in the 880° C. pyrolysate (Table II), only Fraction C in a 0.01% concentration proved to be biologically quite active, while Fraction B had very minor activity. This

TABLE II.—*Polycyclic Composition of 880° C. Pyrolysate of Hot Hexane Extract of Cigarette Tobacco Determined Spectrophotometrically*

Pyrolysate Fraction	
A	Mixture of aliphatic hydrocarbons, naphthalene, mono-substituted aromatics (yellow oil), phenanthrene, 4-methylpyrene, anthracene, pyrene, fluoranthene, and a mixture of unknowns.
B	Unknown (alkyl anthracene), 1:2-cyclopentanophenanthrene, 1:2-benzanthracene, chrysene, acenaphthylene (trace of 3:4-benzpyrene).
C	Perylene, 1:2-benzpyrene, 3:4-benzpyrene, 1:12-benzperylene (total in Fractions C and D), and other polycyclics (Table I).
D	1:12-Benzperylene and other polycyclics.
E	1:2:3:4-Dibenzpyrene, 3:4:8:9-dibenzpyrene, 3:4:9:10-dibenzpyrene, and other polycyclics.
F	1:2:7:8-Dibenzanthracene, 2':3'-naphtho-3:4-pyrene, coronene, and other polycyclics.
G	Coronene, 1:2:5:6-dibenzanthracene, and other polycyclics.
H	Unknown, 3:4-benzpyrene derivative and other polycyclics.
I	A mixture of several unknown polycyclic compounds.

would suggest that the majority of the carcinogenic polycyclics present in tobacco tar chromatograph in the region of benzpyrene.

The identification of 3:4 benzfluoranthene as an active carcinogen represents a case in point. Additional work in which Dr. Hoffmann is engaged concerns studies with radioactive benzpyrene and 1:2:5:6-dibenzanthracene, and is designed to determine the effectiveness of our chemical separation schemes in removing the benzpyrene present in the total tar in the final solutions. Though the higher polynuclear substances are the only carcinogens present in tobacco, they are the major carcinogenic components, and may be regarded as a standard on which to predict the carcinogenic activity of any type of tobacco smoke condensate.

Preventive Approaches

Having determined the major tobacco carcinogens, it now remains to be considered how the carcinogenic activity of tobacco smoke could be most effectively reduced.

Dose-Response Studies

In view of the established principle of carcinogenesis that the higher the dose the greater, up to a given point, the tumour yield, it became pertinent to establish this factor for the experimental animal.[10] In Figs. 2 and 3 we summarize the data in this respect. They indicate that there is a minimum as well as an optimum level at which tobacco smoke condensate produces cancer in the experimental animal, and that the minimum level is about one-third of the optimum level.

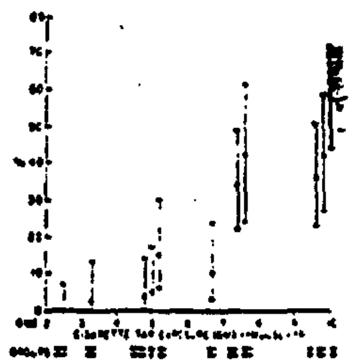

FIG. 2.—Percentage of papillomas by 18 months.

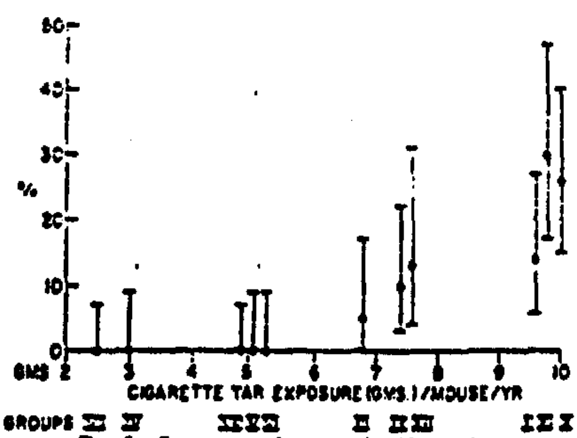

FIG. 3.—Percentage of cancers by 18 months.

These studies are of academic importance in that they demonstrate the reasons why certain investigators may have been unable to produce tumours with tobacco products. More important, they are of practical significance in that they show that if tar exposure is reduced below a certain point the rate of tumour formation, at least in the experimental animal, is

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greatly reduced. In this respect they are similar to the epidemiological studies which show the same relationship. In view of these conclusions it becomes of obvious practical importance to determine ways by which the tar content of the tobacco smoke condensate can be reduced.

Tobacco Types

Considering the possibility that various tobacco types might differ in the production of carcinogenic substances, we undertook a study of cigarettes made of pure Burley, Maryland, Turkish, and Virginia tobaccos.[42] The results of these studies are summarized in Fig. 4, and indicate no significant variation in carcinogenic activity, even though there are obvious variations in nicotine content and thus in the base-free fractions of these tars. These comparisons could be made only for the base-free portion of the tars, since the nicotine content of the Burley tobacco is too high for biological testing. We conclude at the present time that tobacco selection, though it can greatly influence the nicotine content and certainly can also influence the total tar content of the condensate, will not significantly influence the carcinogenic activity of the tar on a gramme-to-gramme basis.

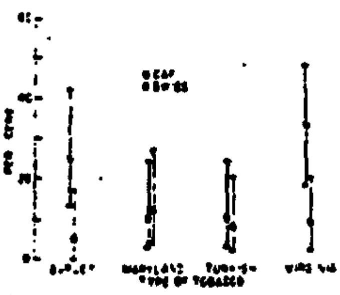

FIG. 4.—Percentage of cancers at 18 months, with different types of tobacco.

Filter Cigarettes

In view of the points emphasized by the dose-response studies, we were interested in conducting studies with filter cigarettes. As summarized in Fig. 5,[31] these studies indicate that on a gramme-to-gramme basis the carcinogenic activity of tar obtained from filter cigarettes is similar to that of unfiltered cigarettes. Therefore it is established that a mechanical filter cannot selectively remove the carcinogenic materials from tobacco smoke, which, knowing the physical make-up of tobacco smoke, could have been predicted. A filter thus serves its purpose not because it removes certain components of tobacco tar selectively, but because it can lower the total tar content of the smoke. Any filter which does not fulfil this requirement is not useful. In the past some tobacco manufacturers, while employing a fairly efficient filter, used high tar-yielding tobaccos. Such smoking products are misleading to the consumer. Tar reduction can be most effectively achieved by a combination of efficient filtration and proper tobacco selection.

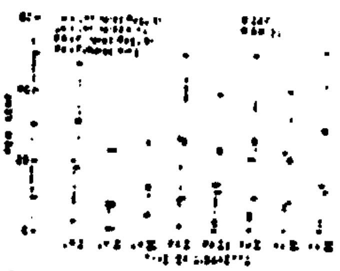

FIG. 5.—Percentage of cancers at 18 months, with different types of cigarette.

Data recently reported showing the tar content of filtered and unfiltered cigarettes as currently smoked in the United States indicate that to-day there is a cognizance of this principle by at least some of the tobacco manufacturers in this country.[44] As indicated in Table III, a marked reduction in some of the major cigarette brands in the United States has taken place. This movement is to be encouraged, and it is hoped that before long all of the tobacco manufacturers in the United States and elsewhere will follow suit. While such a move will not prevent a smoker from developing lung cancer, present evidence indicates that it will reduce his chances of developing this disease.

TABLE III

	1957	1955	Change
*Tar content in mg. of some 85-mm. filter cigarettes**			
Filter A	32·6	29·1	−11%
" B	30·6	[illegible]	−41%
" C	[illegible]	[illegible]	−6%
" D	[illegible]	24·9	−33%
" E	36·3	17·7	−51%
" F (70 mm.)	25·6	15·1	−41%
Tar content in mg. of some 73-mm. regular cigarettes			
Brand A	31·0	[illegible]	−7%
" B	31·5	[illegible]	−9%
" C	[illegible]	33·6	−6%
" D	35·3	[illegible]	−18%
" E	30·9	22·4	−41%
" F (85 mm.)	38·4	37·1	−4%

* Foster D. Snell.[44]

Pyrolysis Studies

In biological experiments we have shown that an extract of tobacco is only weakly carcinogenic compared with tobacco smoke condensate.[41] There is present in unburned tobacco a very small amount of some higher aromatic polycyclics which are apparently formed during the curing process.[1, 37, 38] However, it is clear that the majority of the higher polynuclear substances are formed during the combustion processes of tobacco.

We have set out to undertake a series of studies to determine the temperature ranges at which the majority of the carcinogens are formed. We have pyrolysed hot-hexane-extracted tobacco at temperatures ranging from 880° C. to 560° C. and found that the formation of carcinogens is related to the burning temperature. It does not appear to be so much related to the presence or absence of oxygen, since the activity of the 880° C. pyrolysate in nitrogen and with the addition of oxygen was similar. However, we found that when the temperature was reduced below 700° C. the biological activity was greatly reduced (Fig. 6).[43]

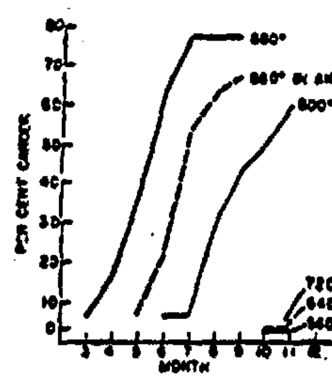

FIG. 6.—Tumour formation in mice upon application of pyrolysis products of hexane extract of tobacco obtained at different temperatures.

We were interested in investigating this problem from a number of different aspects. We smoked cigarettes with a high and a low puff volume in an effort to determine whether this would alter the carcinogenic activity. In view of the fact that maximum temperatures reached in these cigarettes are quite similar, 884° C. ±30° C., we did not expect a variation in activity, and, indeed, none was found.[43] It is of interest in this respect that the cigarettes smoked with a high puff volume yielded more tar. However, all our experiments are based upon a gramme-to-gramme comparison. We

also set out to test whether cigarettes smoked halfway or to the butt end would show different activity, since repyrolysis of condensed tar might produce more carcinogenic material. However, the results again showed a similarity in biological activity even though the tar yield of cigarettes smoked to the very butt end is obviously greater than of those smoked halfway down.[33]

Finally, we have studied the comparative activity of cigar, pipe, and cigarette tars. We found cigar and pipe tar somewhat more active, which, we believe, is due to the fact that cigar and particularly pipe tobacco burns at a high level for a longer period of time than does cigarette tobacco, even though the maximum temperature of cigarettes is higher than that of pipes. These temperature studies have been reported in detail by Touey and Mumpower, and are summarized in Fig 7.[34-44] In burning at a high temperature for a longer period of time the combustion may be more complete in cigars and pipes. Obviously the formation of the carcinogens from organic material is not only a consequence of maximum temperature, but also of the duration of contact with a given temperature level. Present evidence strongly suggests that modification of temperature levels, if achieved, could influence the formation of carcinogens in tobacco.

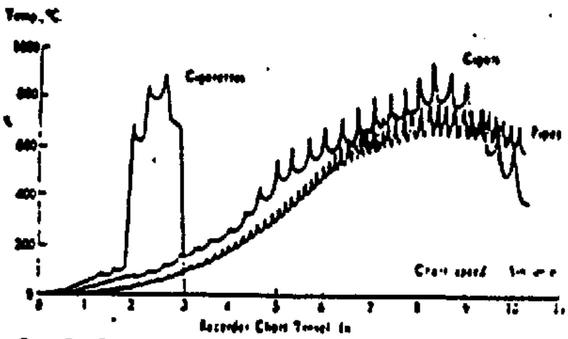

FIG. 7.—Potentiometer graphs (Touey and Mumpower[44 45]).

Study of Precursors

By studying precursors we planned to determine whether there were any components in tobacco smoke condensate which would be particularly susceptible to the formation of higher aromatic polycyclics. We washed tobacco with hot hexane and smoked the extracted tobacco. Of immediate interest is the fact that, though only 5.4% of the tobacco by weight was removed, the tar yield of this cigarette was 35% less than that of an ordinary cigarette.[34] However, on a gramme-to-gramme basis, one of the two experiments showed a somewhat decreased activity and the other showed no decrease in activity from regular tar. Therefore, at present we must conclude that this method cannot effectively reduce the carcinogenic activity of tobacco tar. Lindsey had previously shown some reduction in benzpyrene content of hexane-extracted tobacco.[16] However, our studies do not show a reduction of benzpyrene in hexane-extracted tars.

Lindsey has shown that a large variety of agents present in tobacco can produce higher aromatic polycyclics when pyrolysed.[16] Lam has pyrolysed some of the sterols present in tobacco and has identified higher aromatic polycyclics.[24] We have shown this pyrolysate to be biologically active on mouse skin.[…] In view of these observations it would be most difficult to remove any given substance from tobacco in the absence of which no polycyclics could be formed. We believe, therefore, that even though the different components in tobacco may vary in their relative susceptibility to form higher aromatic polycyclics, a removal of certain substances from the tobacco itself would not be a practical way of reducing its carcinogenic activity upon being smoked.

Practical Preventive Measures

The practical preventive measures as derived from completed laboratory work fall into the following categories.

1. *Lowering of Tar Content in View of Studies on Dose-Response Levels.*—This can be attained through effective filtration and tobacco selection. The greater the decrease in tar content of a given cigarette the lower the liability to cancer development. This is a practical step which can be undertaken by the tobacco industry without delay.

2. *Temperature Reductants.* — We are currently engaged in a study of a number of substances, including aluminium products, to determine whether the temperature of the tobacco during smoking can be lowered sufficiently to influence the formation of polynuclear substances.[33] A number of suggestions have been made to cool the main stream of the smoke. However, since the carcinogens undoubtedly are formed in the burning process, it is here that we must concentrate our efforts.

3. *Modification of Pyrolysis.*—Through the use of a variety of catalysts we are currently engaged in determining whether the polynuclear content of tobacco smoke condensate can be reduced.[33] The idea of catalysts, which is useful in the petroleum industry, may be less applicable in the case of tobacco because of shorter contact time. However, work completed so far suggests that the polynuclear content can be altered. It also seems to affect the proportion of different polynuclear substances. These studies are still in the preliminary stage, and it remains to be determined through combined biological and chemical investigations whether there is a particular catalyst or group of catalysts which could reduce in a practical fashion the carcinogenic activity of the tobacco smoke condensate.

Conclusion

In summary, we have reviewed the work being conducted in various laboratories throughout the world, and particularly in our own laboratory, relating to the tobacco-cancer problem. We have stated the purpose of the laboratory experiment, the direction in which it must go, and have emphasized the relationship that it bears to the human epidemiological study. Like any other phase of scientific investigation, it is the co-operation in different areas of scientific activity which furthers the achievement of a solution to any given problem. While only the epidemiological study can give definite proof of the relationship of smoking and lung cancer, the studies in the laboratory are essential in providing a practical solution to this problem, short of abolishing the smoking habit. Knowing that man will continue to smoke regardless of the evidence, we must expand our laboratory work in order to provide a practical solution to the problem. The thousands of

lives lost in every country each year from cancer of the respiratory tract demands that we expedite our efforts. It is hoped that with the evidence already at hand a practical solution may be within our reach. It is toward this end that laboratory studies involving the smoking-cancer problem must now be directed.

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LUNG CANCER MORTALITY AND THE LENGTH OF CIGARETTE ENDS

AN INTERNATIONAL COMPARISON

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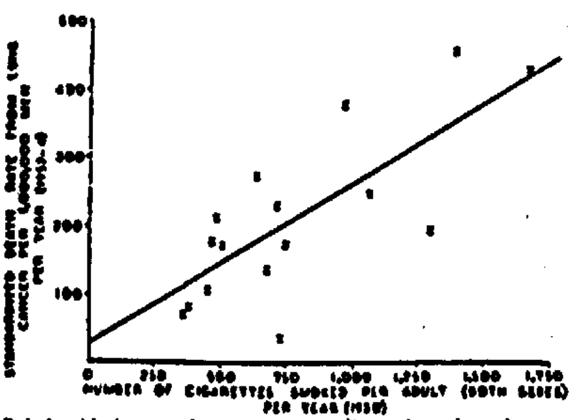
Study of the recorded death rates from lung cancer in different parts of the world shows that there is a fairly close relationship between the present national mortality from the disease and the national consumption of cigarettes 20 to 25 years ago. Data for 16 countries are given in Table I and illustrated in the Chart, in which for each country the standardized mortality of men in 1952–4 is set against the consumption of cigarettes per adult (of both sexes) in 1930. The latter

TABLE I.—*Mortality from Lung Cancer and the Consumption of Cigarettes in 16 Countries**

Standardized Mortality of Men from Cancer of Lung in Years 1952–4. Rate per Million			Cigarette Consumption in Year 1930 (per adult)	Mean Cigarette Consumption (Unweighted)
Mortality Group	Country	Rate		
Over 300	England and Wales	461	1,378	1,330
	Finland	431	1,662	
	Austria	360	960	
200–299	Netherlands	270	632	840
	Belgium	254‡	1,066	
	Switzerland	230*	706	
	New Zealand	216	478	
	U.S.A.	202†	1,296	
100–199	Denmark	179	465	550
	Australia	177	504	
	Canada	176	760	
	France	140	585§	
	Italy	110†	435	
Under 100	Sweden	89*	335	440
	Norway	77	254	
	Japan	40	723	

* The standardized mortality rates were calculated by Segi (1957). Rates for cigarette consumption were given by Todd (1957) or were derived from data for Finland and Norway published by Nielsen and Clemmesen (1954), for Switzerland published by Gsell (1951), and for New Zealand kindly provided by the New Zealand Government, Department of Statistics.
† 1951–3. ‡ 1954. § 1951.



Relationship between lung cancer mortality and previous cigarette consumption in 16 countries. The regression line is given by $y = 0.24x + 26$; the correlation coefficient is 0.76.

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Federal Trade Commission

Report to Congress

For 1994

PURSUANT TO THE FEDERAL CIGARETTE LABELING AND ADVERTISING ACT

ISSUED: 1996

COMMISSION ACTIVITY

On August 11, 1995, the Food and Drug Administration published proposed regulations Restricting the Sale and Distribution of Cigarettes and Smoking Tobacco Products to Protect Children and Adolescents. The FTC submitted a comment that offered general support for FDA's goal of reducing the incidence of underage tobacco use and expressing the Commission's view that the First Amendment gives FDA latitude to impose appropriate advertising restrictions designed to reduce the appeal and use of tobacco products by children and adolescents. The Commission recommended that FDA use the comment period to ensure that its regulations are narrowly tailored to meet First Amendment requirements.

In April 1995, the Commission approved B.A.T Industries' acquisition of The American Tobacco Company after B.A.T agreed to divest itself of certain cigarette brands and a cigarette manufacturing facility. The divestitures must be made to a Commission-approved purchaser, and are intended to preserve the competition that otherwise would have been eliminated by the acquisition. The consent agreement with B.A.T also prohibits B.A.T for a period of ten years from acquiring, without prior Commission approval, interests in any company engaged in the manufacture and sale of cigarettes in the United States. In November 1995, B.A.T requested approval from the Commission to divest certain cigarette brands to Lorillard Tobacco Company. In April 1996, the Commission rejected B.A.T's proposed divestiture, citing concerns that Lorillard would not compete aggressively in the discount market, and that the divestiture in all likelihood would cause a cigarette plant that was part of the proposed divestiture to close. In July 1996, B.A.T applied to divest six of

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PURPOSE

This report is the latest in a series on cigarette sales, advertising, and promotion that the Federal Trade Commission (the Commission) has submitted annually to Congress since 1967 pursuant to the Federal Cigarette Labeling and Advertising Act:[1]

> **The Federal Trade Commission shall transmit a report to the Congress . . . concerning (1) the current practices and methods of cigarette advertising and promotion, and (2) such recommendations for legislation as it may deem appropriate.[2]**

INTRODUCTION

The statistical tables appended to this report provide information on domestic sales, consumption, and advertising and promotional activity for U.S. manufactured cigarettes for the years 1963 through 1994. The tables were compiled from raw data contained in special reports submitted to the Commission pursuant to compulsory process by the five major cigarette manufacturers in the United States: Brown & Williamson Tobacco Corporation, Liggett Group Inc., Lorillard Tobacco Company, Philip Morris Incorporated, and R.J. Reynolds Tobacco Company.[3]

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[1] Pub. L. No. 89-92, 79 Stat. 282 (1965), as amended by Pub. L. No. 98-474, 98 Stat. 2204 (1984) and by Pub. L. No. 99-92, § 11, 99 Stat. 393, 402-04 (1985), current version at 15 U.S.C. § 1331 (1982 & Supp. IV 1986).

[2] 15 U.S.C. § 1337(b) (Supp. IV 1986).

[3] In 1995, B.A.T, the parent corporation of Brown & Williamson, acquired The American Tobacco Company.

the brands in question and the plant to Commonwealth Brands. As of September 1996, the Commission was evaluating that application.

On July 20, 1994, the Commission asked the National Cancer Institute to convene a consensus conference to address certain issues concerning the FTC cigarette testing methodology and ratings system. NCI, which shortly before had received a similar request from then-House Subcommittee Chairman Henry A. Waxman, convened the conference in December 1994. At the close of the conference, the Ad Hoc Committee of the President's Cancer Panel issued a statement recommending, inter alia, that the information currently provided to consumers be expanded to reflect more accurately the tar, nicotine, and carbon monoxide that smokers actually get from the cigarettes they smoke. The Commission is considering the issues raised by the Committee's findings concerning revisions to the FTC test methodology.

DISCUSSION OF THE DATA

Table 1 displays annual cigarette sales by manufacturers to wholesalers and retailers. In 1994, the major domestic cigarette manufacturers sold 490.2 billion cigarettes domestically, which is 28.8 billion more cigarettes than they sold in 1993. This 6.2 percent rise above the 1993 level is the first increase in sales in the last 10 years, and contrasts with an 8.9 percent decrease in sales in 1993. This recent volatility in cigarette sales by manufacturers is not reflected, however, in the cigarette consumption series produced by the U.S. Department of Agriculture (USDA). The USDA consumption estimates for the years 1992 through 1994 are 500 billion, 485 billion, and 486 billion

cigarettes, respectively.[4] Construed together, the two data sets suggest that some increase in the number of cigarettes actually sold to consumers occurred in 1994, but that the dramatic increase reported to the Commission likely reflects, in large part, changes in inventories rather than actual retail sales.

Table 2 shows U.S. adult per capita cigarette sales per year, and is generated by dividing manufacturers' sales to wholesalers and retailers by the U.S. adult population. Per capita sales increased from 2,414 in 1993, to 2,516 in 1994, an increase of 4.2 percent, or 102 cigarettes per person. Per capita sales had declined 9.8 percent, or 261 cigarettes, from 1992 to 1993. As with Table 1, the changes in per capita sales may reflect changes in wholesalers' and retailers' inventories.

Tables 3 through 3E show the amounts spent on cigarette advertising and promotion for the years 1970, and 1975 through 1994.[5] These tables break out the amounts spent on the different types of media advertising (e.g., newspapers and magazines) and sales promotion activities (e.g.,

[4]USDA, Tobacco Situation and Outlook Report, TBS-236, June 1996, Table 1, p. 4. Differences between the FTC and USDA series may reflect changes in inventory holdings by cigarette wholesalers and retailers. Shifts in inventories can influence the numbers of cigarettes sold annually by cigarette manufacturers to wholesalers and retailers, which is the statistic reported to the FTC and contained in the annual cigarette reports. In contrast, year-to-year changes in wholesaler inventories are not reflected in the USDA series, which is based on an estimate of the number of cigarettes actually sold to consumers.

[5]The reported figures include all advertising, merchandising, and promotional expenditures related to cigarettes, regardless of whether such advertising would constitute "commercial speech" or would be protected from law enforcement action under the First Amendment. The Commission began requiring tobacco companies to include expenditures for such protected speech in 1989.

distribution of cigarette samples and specialty gift items) and also give the percentage of the total amount spent for the various types of advertising and promotion.

Table 3E shows that overall, $4.83 billion was spent on cigarette advertising and promotion in 1994, a decrease of $1.2 billion, or 19.9 percent, from the $6.03 billion spent in 1993. This is the first decrease in spending since 1986, when expenditures declined $94.1 million, or 3.8 percent, from the previous year.

Newspaper advertising expenditures decreased 33.3 percent between 1993 and 1994, from $36.2 million to $24.1 million; this advertising category accounts for one-half of 1 percent of all expenditures. There has been a continuing trend away from newspaper advertising since 1981, when newspaper spending accounted for 23.1 percent of total expenditures.

A total of $251.6 million was spent on magazine advertising in 1994, an increase of 7.0 percent from 1993. As a percentage of total advertising, magazine advertising increased from 3.9 to 5.2 percent. Spending on magazine advertising peaked in 1984, when the cigarette companies reported spending $426 million, or 20.3 percent of total advertising and promotional expenditures, for advertising in magazines.

Spending on outdoor advertising totaled $240.0 million in 1994, a slight increase of $8.5 million from 1993, when $231.5 million was spent. In 1994, outdoor advertising expenditures

comprised 5.0 percent of total advertising and promotional spending, down from a high of 15.5 percent in the early 1980's.

Spending on transit advertising decreased from $39.1 million in 1993 to $29.3 million in 1994, a drop of 25.0 percent; however, this category, like newspapers, accounts for only about one-half of 1 percent of all expenditures.

Spending on point-of-sale promotional materials decreased by $58.3 million (14.5 percent) from 1993 ($400.9 million) to 1994 ($342.7 million). As a percentage of total advertising and promotion, point-of-sale advertising has remained near 7 percent since 1988.

Promotional allowances were $1.7 billion in 1994, up 7.8 percent from $1.6 billion in 1993. In 1993, these expenditures accounted for 25.8 percent of the total; they accounted for 34.7 percent of all expenditures for 1994, and for the first time since 1985, this was the largest category of advertising and promotional expenditures.

Money spent giving cigarette samples to the public ("sampling distribution") decreased significantly in 1994. In 1993, $40.2 million was spent on sampling, while in 1994, $7.0 million was spent, a decrease of 82.7 percent. Cigarette sampling distribution accounted for only 0.1 percent of the total spent on advertising and promotion in 1994. Cigarette sampling expenditures reached a high of 7.9 percent of the total spent on advertising and promotion in 1982.

In 1994, $850.8 million was spent on specialty item distribution through the mail, at promotional events, or by any means other than at the point-of-sale with the purchase of cigarettes. This is an increase from 1993 of $95.0 million, and accounted for 17.6 percent of the total advertising and promotional expenditures for 1994. Specialty items distributed along with the purchase of cigarettes were redesignated as retail value added expenses beginning in 1988.[6]

Spending on public entertainment decreased by $3.0 million from 1993 to 1994. With expenditures reported of $81.3 million, public entertainment in 1994 accounted for 1.7 percent of total expenditures.

The cigarette companies reported a total of $31.2 million for direct mail advertising in 1994, virtually no change from the $31.5 million reported in 1993. This category does not include direct mail containing coupons. Coupons sent via direct mail have been reported in the coupon and retail value added category since 1988.

All reporting companies indicated that no money had been spent on endorsements and testimonials for cigarettes in 1994. No expenditures have been reported in this category since 1988.

[6]Specialty item advertising is the practice of branding items such as T-shirts, caps, sunglasses, key chains, calendars, lighters and sporting goods with a brand's logo, and then giving them away or selling them to consumers.

Coupons and retail value added promotions expenditures were cut in half in 1994, dropping $1.31 billion from an all time high of $2.56 billion in 1993 to $1.25 billion in 1994. This 51.2 percent decrease in what had been the largest advertising category since 1990 accounts for almost all of the 19.9 percent overall drop in exnenditures for 1994. This category includes cents-off coupons, multiple pack promotions, and retail value added offers.[7] The cigarette companies were first asked to report these expenses as a distinct category in 1988, when $874 million was spent.

The Commission collects expenditure information in two categories that do not appear as line items on the charts because they may span several categories. In 1988, the Commission began requiring the cigarette companies to state separately the amount of money spent on sports and sporting events. For 1994, the major domestic cigarette companies reported that they spent $76 million on sports and sporting events.[8] This is down by $2 million from 1993 and $6 million from the amount spent in 1992.

In 1989, the Commission began requiring the cigarette companies to declare whether any money or other form of compensation had been paid to have any cigarette brand names or tobacco

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[7]Multiple pack offers are additional packs of cigarettes that are given free with cigarette purchases, such as "buy one, get one free." Retail value added offers include non-cigarette items, such as key chains or lighters, given away at the point of sale with the purchase of cigarettes.

[8]This includes expenditures for: (1) the sponsoring, advertising or promotion of sports or sporting events; support of an individual, group, or sports team; and purchase of or support for equipment, uniforms, sports facilities and/or training facilities; (2) all expenditures for advertising in the name of the cigarette company or any of its brands in a sports facility, on a scoreboard, or in conjunction with the reporting of sports results; and (3) all expenditures for functional promotional items (clothing, hats, etc.) connected with a sporting event.

products appear in any motion pictures or television shows. This practice has been reported as unfunded since 1989.

The data on cigarette advertising and promotional expenditures reported in Tables 3 through 3D were not collected in their present form until 1975. Therefore, Tables 4 and 5, which report cigarette advertising expenditures from 1963 through 1974 and 1970 through 1974, respectively, have been retained in the report for comparative purposes.

Tables 6 through 6C give the domestic market share of, and the percentage of total cigarette advertising expenditures devoted to, cigarettes yielding 15 milligrams (mg) or less tar for the years 1967 through 1994. The data are broken down into separate categories according to tar yields of less than 3, 6, 9, 12, and 15 mg (categories are presented cumulatively).

In 1994, 71.2 percent of the domestic cigarette market was cigarettes yielding 15 mg or less of tar. The market share for cigarettes yielding 15 mg tar or less has increased gradually since 1982, when it accounted for 52.2 percent.

Since 1979, the cigarette companies have reported that the majority of advertising and promotional spending has been devoted to cigarettes yielding 15 mg or less tar. For 1994, they reported that 72.2 percent of all advertising and promotion was spent on cigarettes that yield 15 mg tar or less.

As shown in Table 7, filtered cigarettes have dominated the market since the Commission began collecting this information in 1963, rising from 58 percent at that time to 97 percent in 1992. The market share of filtered cigarettes remained constant in 1994 at 97 percent. Table 8 shows that the cigarette companies have reported a close correlation between advertising and promotion expenditures and domestic market share for filter cigarettes in recent years.

Table 9 provides the domestic market share of the various cigarette length categories. The King-size (79-88 mm) category continues to be the biggest seller, with 56 percent of the market. This category is followed by the Long (94-101 mm) group, which holds 41 percent of the market. Regulars (68-72 mm) and Ultra-Longs (110-121 mm) continued to account for 1 percent and 2 percent, respectively, of the market in 1994.

Tables 10 and 10A provide the domestic market share and percentage of total advertising and promotional expenditures devoted to Long and Ultra-Long cigarettes for 1967 through 1981, and 1982 through 1994, respectively. In 1994, the market share for longer cigarettes decreased slightly (44 percent to 43 percent), while the percentage of total advertising and promotional expenditures rose from 41 percent to 43 percent.

Table 11 gives the market share of menthol and non-menthol cigarettes. In 1994, the market share of menthol cigarettes declined from 26 percent to 25 percent of the market, while non-menthols rose from 74 percent to 75 percent.

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In 1994, the Commission began requiring the cigarette companies to indicate whether "tar" and nicotine ratings were displayed on cigarette packaging and advertising. Table 12 shows that cigarette varieties that printed tar and nicotine ratings on their packs represented only 6.3 percent of the overall market. Table 12 also shows: (1) the percentage of the overall cigarette market represented by varieties with different tar ratings, and (2) within each tar group, the market share of those varieties that disclose tar and nicotine ratings on their packs.

TABLE I
DOMESTIC CIGARETTE SALES
(BILLIONS OF CIGARETTES)

YEAR	TOTAL SALES	UNIT CHANGE FROM PRIOR YEAR	% CHANGE FROM PRIOR YEAR
1963	516.5	—	—
1964	505.0	(11.5)	(2.2)
1965	521.1	16.1	3.2
1966	529.9	8.8	1.7
1967	525.8	5.9	1.1
1968	540.3	4.5	.8
1969	527.9	(12.4)	(2.3)
1970	534.2	6.3	1.1
1971	547.2	13.0	2.4
1972	561.7	14.5	2.7
1973	584.7	23.0	4.1
1974	594.5	9.8	1.7
1975	603.2	8.7	1.5
1976	609.9	6.7	1.1
1977	612.6	2.7	.4
1978	615.3	2.7	.4
1979	621.8	6.5	1.1
1980	628.2	6.4	1.0
1981	636.5	8.3	1.3
1982	632.5	(4.0)	(.6)
1983	603.6	(28.9)	(4.6)
1984	608.4	4.8	.8
1985	599.3	(9.1)	(1.5)
1986	586.4	(12.9)	(2.2)
1987	575.4	(11.0)	(1.9)
1988	560.7	(14.7)	(2.6)
1989	525.6	(35.1)	(6.3)
1990	523.7	(1.9)	(.4)
1991	510.9	(12.8)	(2.4)
1992	506.4	(4.5)	(.9)
1993	[illegible]	[illegible]	(8.9)
1994	490.2	[illegible]	6.2

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TABLE 2

PER CAPITA CONSUMPTION

All U.S. Residents and Overseas Military Personnel
18 years of Age and Older*

YEAR	CIGARETTES
1963	4,286
1964	4,143
1965	4,196
1966	4,197
1967	4,175
1968	4,145
1969	3,986
1970	3,969
1971	3,982
1972	4,018
1973	4,112
1974	4,110
1975	4,095
1976	4,068
1977	4,015
1978	3,965
1979	3,937
1980	3,858
1981	3,818
1982	3,733
1983	3,513
1984	3,497
1985	3,400
1986	3,288
1987	3,190
1988	3,073
1989	2,846
1990	2,829
1991	2,724
1992	2,675
1993	2,414
1994	2,516

*Population data used in compiling the 1994 figures include U.S. residents age 18 and older and overseas military personnel as of October 1, 1994. Source of population figure is the U.S. Department of Commerce, Bureau of Census.

TABLE 3

DOMESTIC CIGARETTE ADVERTISING AND PROMOTIONAL EXPENDITURES
FOR YEARS 1970, 1975-1977
(THOUSANDS OF DOLLARS)

TYPE OF ADVERTISING	1970	% OF TOTAL	1975	% OF TOTAL
Newspapers	$14,026	3.9	$104,460	21.3
Magazines	50,018	13.9	131,199	26.6
Outdoor	7,338	2.0	84,329	17.2
Transit	5,354	1.5	10,852	2.2
Point of Sale	11,663	3.2	35,317	7.2
Promotional Allowances	33,789	9.4	72,018	14.7
Sampling Distribution	11,775	3.3	24,196	4.9
Specialty Item Distribution	5,652	2.6	10,088	2.1
Public Entertainment	544	0.2	8,484	1.7
All Others*	220,841	61.1	10,311	2.0
Total**	$361,000	100.0	$491,254	100.0

TYPE OF ADVERTISING	1976	% OF TOTAL	1977	% OF TOTAL
Newspapers	$155,808	24.4	$190,677	24.5
Magazines	148,032	23.2	173,296	22.2
Outdoor	102,689	16.1	120,338	15.4
Transit	19,341	3.0	21,530	2.8
Point of Sale	44,176	6.9	46,220	5.9
Promotional Allowance	82,523	12.9	108,227	13.9
Sampling Distribution	40,390	6.3	47,683	6.1
Specialty Item Distribution	20,030	3.[illegible]	35,797	4.6
Public Entertainment	7,946	1.[illegible]	9,538	1.2
All Others*	18,182	2.8	26,157	3.4
Total**	$639,117	100.0	$779,463	100.0

* Includes TV and Radio advertising expenditures of $207,324,000 and $12,492,000, respectively, for 1970. Broadcast advertising was banned after January 1, 1971. Expenditures for direct mail, endorsements, testimonials, and audio-visual are included in the "All Others" category to avoid disclosure of individual company data.

** Because of rounding, sums of percentages may not equal 100 percent.

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TABLE 3A

DOMESTIC CIGARETTE ADVERTISING AND PROMOTIONAL EXPENDITURES FOR YEARS 1978-1981 (THOUSANDS OF DOLLARS)

TYPE OF ADVERTISING	1978	% OF TOTAL	1979	% OF TOTAL
Newspapers	$186,947	21.4	$240,978	22.2
Magazines	184,236	21.1	257,715	23.8
Outdoor	149,010	17.0	162,966	15.0
Transit	22,899	2.6	21,151	2.0
Point of Sale	57,384	6.6	66,096	6.1
Promotional Allowances	125,148	14.3	137,111	12.7
Sampling Distribution	47,376	5.4	64,286	5.9
Specialty Item Distribution	48,281	5.5	62,029	5.7
Public Entertainment	11,590	1.3	10,783	1.0
All Others*	42,100	4.8	60,310	5.6
Total**	$874,971	100.0	$1,083,425	100.0

TYPE OF ADVERTISING	1980	% OF TOTAL	1981	% OF TOTAL
Newspapers	$304,380	24.5	$358,096	23.1
Magazines	266,208	21.4	291,227	18.8
Outdoor	193,333	15.6	228,081	14.7
Transit	26,160	2.1	21,931	1.4
Point of Sale	79,799	6.4	98,968	6.4
Promotional Allowances	179,094	14.4	229,077	14.8
Sampling Distribution	50,459	4.1	81,522	5.3
Specialty Item Distribution	69,248	5.6	115,107	7.5
Public Entertainment	16,914	1.4	37,423	2.4
All Others*	56,694	4.6	86,226	5.6
Total**	$1,242,289	100.0	$1,547,658	100.0

* Expenditures for direct mail, endorsements, testimonials, and audio-visual are included in the "All Others" category to avoid disclosure of individual company data.

** Because of rounding, sums of percentages may not equal 100 percent.

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TABLE 3B

DOMESTIC CIGARETTE ADVERTISING AND PROMOTIONAL EXPENDITURES
FOR THE YEARS 1982-1985
(THOUSANDS OF DOLLARS)

TYPE OF ADVERTISING	1982	% OF TOTAL	1983	% OF TOTAL
Newspapers	$282,897	15.8	$200,563	10.6
Magazines	349,229	19.5	388,365	20.4
Outdoor	266,925	14.9	295,226	15.5
Transit	24,135	1.3	26,652	1.4
Point of Sale	116,954	6.5	170,059	8.9
Promotional Allowances	272,269	15.2	366,153	19.3
Sampling Distribution	141,178	7.9	125,968	6.6
Specialty Item Distribution	95,246	5.3	127,186	6.6
Public Entertainment	63,168	3.5	76,648	4.0
All Others*	181,813	10.1	123,951	6.5
Total**	$1,793,814	100.0	$1,900,771	100.0

TYPE OF ADVERTISING	1984	% OF TOTAL	1985	% OF TOTAL
Newspapers	$193,519	9.2	$203,527	8.2
Magazines	425,912	20.3	395,129	16.0
Outdoor	284,927	13.6	300,233	12.1
Transit	25,817	1.2	33,136	1.3
Point of Sale	167,279	8.0	142,921	5.8
Promotional Allowances	363,247	17.3	548,877	22.2
Sampling Distribution	148,031	7.1	140,5[illegible]	5.7
Specialty Item Distribution	140,431	6.7	211,429	8.5
Public Entertainment	59,988	2.9	57,581	2.3
All Others*	286,035	13.7	443,043	17.9
Total**	$2,095,231	100.0	$2,476,441	100.0

* Expenditures for direct mail, endorsements, testimonials, and audio-visual are included in the "All Others" category.

** Because of rounding, sums of percentages may not equal 100 percent.

51676 0507

TABLE 3C

DOMESTIC CIGARETTE ADVERTISING AND PROMOTIONAL EXPENDITURES
FOR YEARS 1986-1989
(THOUSANDS OF DOLLARS)

TYPE OF ADVERTISING	1986	% OF TOTAL	1987	% OF TOTAL
Newspapers	$119,629	5.0	$95,810	3.7
Magazines	340,160	14.3	317,748	12.3
Outdoor	301,822	12.7	269,778	10.5
Transit	34,725	1.5	35,822	1.4
Point of Sale	135,541	5.7	153,494	5.9
Promotional Allowances	630,036	26.4	702,430	27.2
Sampling Distribution	98,866	4.1	55,020	2.1
Specialty Item Distribution	210,128	8.8	391,351	15.2
Public Entertainment	71,439	3.0	71,389	2.8
Direct Mail	187,057	7.9	187,931	7.3
Endorsements and Testimonials	384	—	376	—
All Others*	252,570	10.0	299,355	11.6
Total**	$2,382,357	100.0	$2,580,504	100.0

TYPE OF ADVERTISING	1988	% OF TOTAL	1989	% OF TOTAL
Newspapers	$105,783	3.2	$76,993	2.1
Magazines	355,055	10.8	380,393	10.5
Outdoor	319,293	9.7	358,583	9.9
Transit	44,379	1.4	52,294	1.4
Point of Sale	222,289	6.8	241,809	6.7
Promotional Allowances	879,703	26.9	999,843	27.6
Sampling Distribution	7[illegible]511	[illegible]	57,771	1.6
Specialty Item Distribution	190,003	5.8	262,432	7.3
Public Entertainment	88,072	2.7	92,120	2.5
Direct Mail	42,545	1.3	45,498	1.3
Endorsements and Testimonials	781	—	—	—
Coupons and Retail Value Added	874,127	26.7	959,965	26.5
All Others*	78,366	2.4	89,290	2.5
Total**	$3,274,853	100.0	$3,616,993	100.0

*Expenditures for audio-visual are included in the "All Others" category to avoid disclosure of individual company data.

**Because of rounding, sums of percentages may not equal 100 percent.

51676 0508

TABLE 3D

DOMESTIC CIGARETTE ADVERTISING AND PROMOTIONAL EXPENDITURES
FOR YEARS 1990-1993
(THOUSANDS OF DOLLARS)

TYPE OF ADVERTISING	1990	% OF TOTAL	1991	% OF TOTAL
Newspapers	$71,174	1.8	48,212	1.0
Magazines	328,143	8.2	278,110	6.0
Outdoor	375,627	9.4	386,165	8.3
Transit	60,249	1.5	60,163	1.3
Point of Sale	303,855	7.6	344,580	7.4
Promotional Allowances	1,021,427	25.6	1,156,280	24.9
Sampling Distribution	100,893	2.5	56,970	1.2
Speciality Item Distribution	307,037	7.7	184,348	4.0
Public Entertainment	125,094	3.1	118,622	2.6
Direct Mail	51,875	1.3	65,002	1.4
Endorsements/Testimonials	—	—	—	—
Coupons and Retail Value Added	1,183,798	29.6	1,882,905	40.4
All Others*	62,917	1.6	68,758	1.5
Total**	$3,992,008	100.0	4,650,114	100.0

TYPE OF ADVERTISING	1992	% OF TOTAL	1993 ***	% OF TOTAL
Newspapers	$35,467	.7	36,220	.6
Magazines	237,061	4.5	235,253	3.9
Outdoor	295,657	5.7	231,481	3.8
Transit	53,293	1.0	39,117	.6
Point of Sale	366,036	7.0	400,943	6.6
Promotional Allowances	1,514,026	28.9	1,557,635	25.8
Sampling Distribution	49,315	.9	40,202	.7
Speciality Item Distribution	339,997	6.5	755,780	12.5
Public Entertainment	89,739	1.7	84,276	1.4
Direct Mail	34,345	.7	31,463	.5
Endorsements/Testimonials	—	—	—	—
Coupons and Retail Value Added	2,175,373	41.6	2,559,387	42.4
All Others*	41,608	.8	63,680	1.2
Total**	$5,231,917	100.0	6,035,437	100.0

*Expenditures for audio-visual are included in the "All Others" category to avoid disclosure of individual company data.

**Because of rounding, sums of percentages may not equal 100 percent.

***1993 data have been revised from totals previously reported to reflect company revisions submitted to the FTC in 1995.

TABLE 3E

DOMESTIC CIGARETTE ADVERTISING AND PROMOTIONAL EXPENDITURES
FOR YEAR 1994
(THOUSANDS OF DOLLARS)

TYPE OF ADVERTISING	1994	% OF TOTAL
Newspapers	$24,143	.5
Magazines	251,644	5.2
Outdoor	240,024	5.0
Transit	29,323	.6
Point of Sale	342,650	7.1
Promotional Allowances	1,678,917	34.7
Sampling Distribution	6,974	.1
Speciality Item Distribution	850,810	17.6
Public Entertainment	81,292	1.7
Direct Mail	31,187	.7
Endorsements/Testimonials	---	---
Coupons and Retail Value Added	1,248,896	25.8
All Others*	47,672	1.0
Total**	$4,833,532	100.0

*Expenditures for audio-visual are included in the "All Others" category to avoid disclosure of individual company data.

**Because of rounding, sums of percentages may not equal 100 percent.

51676 0510

TABLE 4

DOMESTIC CIGARETTE ADVERTISING EXPENDITURES
BY MEDIA FOR YEARS 1963 - 1974*
(MILLIONS OF DOLLARS)

YEAR	TV	NEWSPAPER MAGAZINES	RADIO	DIRECT	OTHER	TOTAL
1963	$151.7	45.6	31.6	13.2	7.4	249.5
1964	170.2	45.2	25.5	14.6	5.8	261.3
1965	175.6	41.9	24.8	14.7	6.0	263.0
1966	198.0	43.4	31.3	17.9	6.9	297.5
1967	226.9	41.2	17.5	20.3	6.0	311.5
1968	217.2	44.6	21.3	21.6	6.0	310.7
1969	221.3	48.7	13.6	13.4	8.9	305.9
1970	205.0	64.2	12.4	16.9	16.2	314.7
1971	2.2	157.6	0	27.0	64.8	251.6
1972	0	159.2	0	22.9	75.5	257.6
1973	0	157.7	0	15.2	74.6	247.5
1974	0	195.1	0	31.1	80.6	306.8

*The data reported in Tables 3 through 3D were not collected in their present form until 1975. Thus, Tables 4 and 5, which report cigarette advertising expenditures from 1963 through 1974 and from 1970 through 1974, respectively, have been retained in this report for comparative purposes.

51676 0511

TABLE 5

DOMESTIC CIGARETTE ADVERTISING EXPENDITURES
BY MEDIA FOR YEARS 1970 - 1974*
(MILLIONS OF DOLLARS)

YEAR	TV	RADIO	NEWSPAPER	MAGAZINES	OUTDOOR/ TRANSIT	DIRECT	OTHER	TOTAL
1970	$205.0	$12.4	$14.7	$49.5	$11.7	$16.9	$4.5	$314.7
1971	2.2	0	59.3	98.3	60.6	27.0	4.2	251.6
1972	0	0	63.1	96.1	67.5	22.9	8.0	257.6
1973	0	0	65.3	92.4	63.2	15.2	11.4	247.5
1974	0	0	80.5	114.6	71.4	31.1	9.2	306.8

*The data reported in Tables 3 through 3D were not collected in their present form until 1975. Thus, Tables 4 and 5, which report cigarette advertising expenditures from 1963 through 1974 and from 1970 through 1974, respectively, have been retained in this report for comparative purposes.

51676 0512

TABLE 6

DOMESTIC MARKET SHARE OF AND EXPENDITURES FOR ADVERTISING AND OTHER PROMOTIONAL ACTIVITIES FOR CIGARETTES YIELDING FIFTEEN MILLIGRAMS (mg.) OR LESS OF TAR
(1967 - 1981)

YEAR	DOMESTIC MARKET SHARE CIGARETTES YIELDING 15 mg. OR LESS TAR	PERCENTAGE OF TOTAL EXPENDITURES* FOR ADVERTISING AND OTHER PROMOTIONAL ACTIVITIES DEVOTED TO CIGARETTES YIELDING 15 mg. OR LESS TAR
1967	2.0%	5.5%
1968	2.5%	9.2%
1969	3.0%	12.7%
1970	3.6%	10.5%
1971	3.8%	9.3%
1972	6.6%	15 1%
1973	8.9%	17.8%
1974	8.9%	15.2%
1975	13.5%	19.6%
1976	15.9%	39.6%
1977	22.7%	49.4%
1978	27.5%	48.1%
1979	40.9%	66.9%
1980	44.8%	65.1%
1981	56.0%	70.8%

*Promotional activities, which the reporting companies did not consider to be "advertising," are not included in the data for years prior to 1975.

TABLE 6A

DOMESTIC MARKET SHARE OF AND EXPENDITURES FOR ADVERTISING AND OTHER PROMOTIONAL ACTIVITIES FOR CIGARETTES YIELDING FIFTEEN MILLIGRAMS (mg.) OR LESS OF TAR (1982 - 1987)

	1982 MARKET SHARE	1982 PERCENTAGE OF TOTAL ADVERTISING EXPENDITURES	1983 MARKET SHARE	1983 PERCENTAGE OF TOTAL ADVERTISING EXPENDITURES
15 mg. or less tar	52.2%	64.3%	53.1%	67.4%
12 mg. or less tar	43.8%	57.8%	44.9%	58.8%
9 mg. or less tar	27.8%	41.4%	27.9%	35.1%
6 mg. or less tar	8.9%	15.6%	9.4%	15.7%
3 mg. or less tar	2.9%	5.7%	3.1%	4.2%

	1984 MARKET SHARE	1984 PERCENTAGE OF TOTAL ADVERTISING EXPENDITURES	1985 MARKET SHARE	1985 PERCENTAGE OF TOTAL ADVERTISING EXPENDITURES
15 mg. or less tar	51.0%	57.1%	51.9%	59.0%
12 mg. or less tar	43.4%	51.7%	43.1%	46.9%
9 mg. or less tar	26.3%	33.4%	25.3%	30.1%
6 mg. or less tar	9.4%	12.3%	8.4%	9.5%
3 mg. or less tar	2.9%	4.3%	2.3%	3.1%

	1986 MARKET SHARE	1986 PERCENTAGE OF TOTAL ADVERTISING EXPENDITURES	1987 MARKET SHARE	1987 PERCENTAGE OF TOTAL ADVERTISING EXPENDITURES
15 mg. or less tar	52.6%	61.9%	55.4%	64.4%
12 mg. or less tar	44.5%	53.4%	47.8%	54.3%
9 mg. or less tar	22.3%	26.1%	20.2%	26.7%
6 mg. or less tar	9.9%	11.5%	10.0%	11.9%
3 mg. or less tar	2.6%	3.8%	2.5%	3.3%

51676 0514

TABLE 6B

DOMESTIC MARKET SHARE OF AND EXPENDITURES FOR ADVERTISING AND OTHER PROMOTIONAL ACTIVITIES FOR CIGARETTES YIELDING FIFTEEN MILLIGRAMS (mg.) OR LESS OF TAR (1988 - 1993)

	1988 MARKET SHARE	1988 PERCENTAGE OF TOTAL ADVERTISING EXPENDITURES	1989 MARKET SHARE	1989 PERCENTAGE OF TOTAL ADVERTISING EXPENDITURES
15 mg. or less tar	54.2%	60.7%	55.1%	62.6%
12 mg. or less tar	48.7%	54.4%	48.4%	53.6%
9 mg. or less tar	20.1%	26.1%	21.5%	27.2%
6 mg. or less tar	10.7%	12.9%	11.4%	13.0%
3 mg. or less tar	3.1%	4.2%	2.4%	2.8%

	1990 MARKET SHARE	1990 PERCENTAGE OF TOTAL ADVERTISING EXPENDITURES	1991 MARKET SHARE	1991 PERCENTAGE OF TOTAL ADVERTISING EXPENDITURES
15 mg. or less tar	60.6%	68.6%	60.5%	64.0%
12 mg. or less tar	51.5%	55.4%	52.6%	53.9%
9 mg. or less tar	25.5%	30.3%	22.0%	23.7%
6 mg. or less tar	12.2%	12.6%	12.7%	12.8%
3 mg. or less tar	2.8%	2.5%	2.6%	2.6%

	1992 MARKET SHARE	1992 PERCENTAGE OF TOTAL ADVERTISING EXPENDITURES	1993 MARKET SHARE	1993 PERCENTAGE OF TOTAL ADVERTISING EXPENDITURES
15 mg. or less tar	68.7%	71.3%	66.5%	65.9%
12 mg. or less tar	52.9%	55.7%	53.3%	54.8%
9 mg. or less tar	24.9%	27.3%	23.4%	20.8%
6 mg. or less tar	12.7%	13.3%	12.6%	12.4%
3 mg. or less tar	2.5%	2.3%	1.9%	3.7%

51676 0515

TABLE 6C

DOMESTIC MARKET SHARE OF AND EXPENDITURES FOR ADVERTISING AND OTHER PROMOTIONAL ACTIVITIES FOR CIGARETTES YIELDING FIFTEEN MILLIGRAMS (mg.) OR LESS OF TAR (1994)

	1994 MARKET SHARE	1994 PERCENTAGE OF TOTAL ADVERTISING EXPENDITURES
15 mg. or less tar	71.2%	72.1%
12 mg. or less tar	53.7%	54.5%
9 mg. or less tar	23.1%	20.9%
6 mg. or less tar	12.3%	11.0%
3 mg. or less tar	2.1%	1.4%

51676 0516

TABLE 7

DOMESTIC MARKET SHARE OF FILTER AND NON-FILTER CIGARETTES

YEAR	NON-FILTER	FILTER	CHARCOAL	NON-CHARCOAL
1963	42%	[illegible]	[illegible]	*
1964	39%	61%	[illegible]	*
1965	36%	64%	[illegible]	*
1966	32%	[illegible]	*	*
1967	28%	72%	*	*
1968	26%	74%	6%	68%
1969	23%	77%	6%	71%
1970	20%	80%	6%	74%
1971	18%	82%	6%	76%
1972	16%	84%	6%	87%
1973	15%	85%	5%	80%
1974	14%	86%	5%	81%
1975	13%	87%	5%	82%
1976	12%	88%	4%	84%
1977	10%	90%	4%	86%
1978	10%	90%	3%	87%
1979	9%	91%	3%	88%
1980	8%	92%	3%	89%
1981	8%	92%	2%	90%
1982	7%	93%	2%	91%
1983	7%	93%	2%	91%
1984	7%	93%	2%	91%
1985	6%	94%	1%	93%
1986	6%	94%	1%	93%
1987	4%	96%	**	**
1988	5%	95%	**	**
1989	5%	95%	**	**
1990	5%	[illegible]	**	**
1991	4%	96%	**	**
1992	3%	97%	**	**
1993	3%	97%	**	**
1994	3%	97%	**	**

* Figures for charcoal filter cigarettes for the years 1963 through 1967 were not obtained.

** Beginning with 1987, figures for charcoal filter cigarettes have no longer been reported.

51676 0517

TABLE 8

DOMESTIC MARKET SHARE OF AND EXPENDITURES
FOR ADVERTISING AND OTHER PROMOTIONAL ACTIVITIES
FOR FILTER CIGARETTES

YEAR	DOMESTIC MARKET SHARE OF FILTER CIGARETTES	PERCENTAGE OF TOTAL EXPENDITURES FOR ADVERTISING AND OTHER PROMOTIONAL ACTIVITIES DEVOTED TO FILTER CIGARETTES*
1963	58%	75%
1964	61%	78%
1965	64%	77%
1966	68%	75%
1967	72%	95%
1968	74%	95%
1969	77%	97%
1970	80%	98%**
1971	82%	98%
1972	84%	99%
1973	85%	98%
1974	86%	98%
1975	87%	98%
1976	88%	99%
1977	90%	99%
1978	90%	99%
1979	91%	99%
1980	92%	96%
1981	92%	96%
1982	93%	96%
1983	93%	96%
1984	93%	96%
1985	94%	96%
1986	94%	96%
1987	95%	97%
1988	95%	97%
1989	95%	96%
1990	95%	96%
1991	96%	96%
1992	97%	97%
1993	97%	97%
1994	97%	98%

*Promotional activities, which the reporting companies did not consider to be "advertising," are not included in the data for years prior to 1975.

**If the above 1970 figure were recomputed from data received in 1978, the 1970 figure would be 96%. The change would be due primarily to the inclusion of the promotional allowance in data received in 1978 for 1970 and not reflected in the computations resulting in the original 1970 figures.

TABLE 9

DOMESTIC MARKET SHARE OF CIGARETTES
BY LENGTH IN MILLIMETERS (mm)

YEAR	68-72mm	79-88mm	94-101mm	110-121mm
1967	14%	77%	9%	---
1968	12%	74%	13%	--- *
1969	11%	74%	16%	--- *
1970	9%	73%	18%	---
1971	8%	72%	20%	---
1972	8%	71%	21%	---
1973	7%	71%	22%	---
1974	6%	71%	23%	--- **
1975	6%	69%	24%	1%
1976	5%	69%	24%	2%
1977	5%	67%	26%	2%
1978	5%	65%	27%	2% *
1979	4%	65%	30%	2% *
1980	3%	63%	32%	2%
1981	3%	62%	33%	2%
1982	3%	61%	34%	2%
1983	3%	60%	34%	2%
1984	3%	59%	36%	2%
1985	3%	58%	37%	2%
1986	2%	58%	37%	3%
1987	2%	57%	38%	3%
1988	2%	57%	38%	2%
1989	2%	57%	39%	2%
1990	2%	57%	39%	2%
1991	2%	56%	40%	2%
1992	2%	56%	41%	2% *
1993	1%	55%	42%	2%
1994	1%	56%	41%	2%

*Because of rounding, the total of the individual percentages may not equal 100 percent in some instances.

**The 110-121 mm length was combined with 94-101 mm length.

51676 0519

TABLE 10

DOMESTIC MARKET SHARE OF AND EXPENDITURES FOR ADVERTISING AND OTHER PROMOTIONAL ACTIVITIES FOR LONGER (94-121 mm) CIGARETTE VARIETIES (1967 - 1981)

YEAR	DOMESTIC MARKET SHARE OF LONGER CIGARETTES	PERCENTAGE OF TOTAL EXPENDITURES FOR ADVERTISING AND OTHER PROMOTIONAL ACTIVITIES DEVOTED TO LONGER CIGARETTES
1967	9%	39%
1968	13%	39%
1969	16%	33%
1971	20%	30%
1972	21%	32%
1973	22%	29%
1974	23%	46%
1975	95-101 mm 24%) 110-112mm 1%) 25%	95-101 mm 18%) 110-121mm 11%) 29%
1976	95-101 mm 24%) 110-121mm 2 %) 26%	95-101 mm 19%) 110-121mm 7%) 26%
1977	95-101 mm 26%) 110-121mm 2%) 28%	95-101 mm 25%) 110-121mm 3%) 28%
1978	95-101 mm 27%) 110-121mm 3%) 30%	95-101 mm 32%) 110-121mm 2%) 34%
1979	95-101 mm 30%) 110-121mm 2%) *32%	95-101 mm 32%) 110-121mm 2%) 34%
1980	94-101 mm 32%) 110-121mm 2%) 34%	94-101 mm 34%) 110-121mm 2%) 36%
1981	94-101 mm 33%) 110-121mm 2%) 35%	94-101 mm 30%) 110-121mm 5%) 35%

*If the above 1970 figure were recomputed from data received in 1978, the 1970 figure would be 27%. The change would be due primarily to the inclusion of the promotional allowance in data received in 1978 for 1970 and not reflected in the computations resulting in the original 1970 figure.

51676 0520

TABLE 10A

DOMESTIC MARKET SHARE OF AND EXPENDITURES FOR ADVERTISING AND OTHER PROMOTIONAL ACTIVITIES FOR LONGER (92-121 mm) CIGARETTE VARIETIES (1982 - 1994)

YEAR	DOMESTIC MARKET SHARE OF LONGER CIGARETTES	PERCENTAGE OF TOTAL EXPENDITURES FOR ADVERTISING AND OTHER PROMOTIONAL ACTIVITIES DEVOTED TO LONGER CIGARETTES
1982	92-101mm 34%) 110-121mm 2%) 36%	92-101mm 39%) 110-121mm 2%) 41%
1983	92-101mm 34%) 110-121mm 2%) 36%	92-101mm 35%) 110-121mm 3%) 38%
1984	92-101mm 36%) 110-121mm 2%) 38%	92-101mm 40%) 110-121mm 3%) 43%
1985	92-101mm 37%) 110-121mm 2%) 39%	92-101mm 41%) 110-121mm 3%) 44%
1986	92-101mm 37%) 110-121mm 3%) 40%	92-101mm 42%) 110-121mm 3%) 45%
1987	92-101mm 38%) 110-121mm 3%) 41%	92-101mm 45%) 110-121mm 3%) 48%
1988	92-101mm 38%) 110-121mm 3%) 41%	92-101mm 43%) 110-121mm 2%) 45%
1989	92-101mm 39%) 110-121mm 2%) 41%	92-101mm 44%) 110-121mm 2%) 46%
1990	92-101mm 39%) 110-121mm 2%) 41%	92-101mm 43%) 110-121mm 2%) 45%
1991	92-101mm 40%) 110-121mm 2%) 42%	92-101mm 42%) 110-121mm 2%) 44%
1992	92-101mm 41%) 110-121mm 2%) 43%	92-101mm 44%) 110-121mm 2%) 46%
1993	92-101mm 42%) 110-121mm 2%) 44%	92-101mm 39%) 110-121mm 2%) 41%
1994	92-101mm 41%) 110-121mm 2%) 43%	92-101mm 41%) 110-121mm 2%) 43%

51676 0521

TABLE 11

DOMESTIC MARKET SHARE OF MENTHOL
AND NON-MENTHOL CIGARETTES

YEAR	MENTHOL	NON-MENTHOL
1963	16%	84%
1964	16%	84%
1965	18%	82%
1966	19%	81%
1967	20%	80%
1968	21%	79%
1969	22%	78%
1970	23%	77%
1971	24%	76%
1972	24%	76%
1973	25%	75%
1974	27%	73%
1975	27%	73%
1976	28%	72%
1977	28%	72%
1978	28%	72%
1979	29%	71%
1980	28%	72%
1981	28%	72%
1982	29%	71%
1983	28%	72%
1984	28%	72%
1985	28%	72%
1986	28%	72%
1987	28%	72%
1988	28%	72%
1989	27%	73%
1990	26%	74%
1991	27%	73%
1992	26%	74%
1993	26%	74%
1994	25%	75%

TABLE 12

DISCLOSURE OF TAR AND NICOTINE RATINGS
ON CIGARETTE PACKS
(1994 DATA)

Overall market share of cigarette varieties that disclose ratings on the cigarette pack: 6.3 percent.

tar rating of cigarette variety	market share of varieties in tar group	market share of varieties in tar group that disclose ratings on pack
more than 15 mg. tar	28.8%	0.0%
12-15 mg. tar	19.3%	0.0%
8-11 mg. tar	39.6%	2.4%
4-7 mg. tar	11.2%	30.8%
3 mg. or less tar	2.1%	91.8%
	100%	

51676 0523

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51676 0524

RJR Nabisco Fourth Quarter Report

January 28, 1997

Dear Fellow Shareholder:

I am very pleased to report that RJR Nabisco posted exceptionally strong financial results in the fourth quarter, with earnings up in each of our major businesses — international tobacco, domestic tobacco and food — and the outlook is bright for a strong performance in 1997.

Absent one-time items in the fourth quarter of both years:

- Fully diluted net income per share rose 22% to \$.73;
- Net income rose 20% to \$248 million;
- Operating company profit increased 11% to \$923 million;
- Cash net income available to common rose 14% to \$372 million;
- International tobacco sales rose 19%, operating company profit rose 10%;
- Domestic tobacco sales were stable and operating company profit rose 2%; and
- Food sales rose 6% and operating company profit rose 19%.

This was an outstanding quarter for the company by virtually any measure. Our 22 percent earnings gain underscores the progress the company is making reinvigorating the international tobacco and food businesses and stabilizing the performance of the domestic tobacco business.

Full-year results are included in more detail in the financial highlights of this report. Absent one-time items, results were strong, with fully diluted net income per share up 14 percent to \$2.62, operating company contribution up 6 percent to \$3.41 billion and net sales up 7 percent to \$17 billion.

When I was named your company's chief executive last year, I stressed how important it would be for RJR Nabisco to meet its commitments to perform for shareholders. We've now had four consecutive quarters of exceeding Wall Street earnings expectations. Simply put, your company is beginning to demonstrate that it has the ability to meet its earnings commitments consistently.

As we move forward, the packaged goods industry is confronting many competitive challenges and a number of companies have seen their financial performance slip in recent quarters. We consider it a top priority to continue to improve our financial performance as we move into 1997, and I see no reason why the company can't build on the momentum of 1996 and add value to your investment.

Ongoing Legal and Public Policy Challenges

The environment for the domestic tobacco business continues to be challenging, particularly on the legal and public policy fronts. As I've noted before, the uncertainties associated with the current external environment have led Wall Street to put a minimal value on domestic tobacco businesses, including ours.

Our biggest challenge as a company is to reduce that level of uncertainty and enable investors to appropriately value the \$1.4 billion annual earnings stream of our domestic tobacco company. We should be able to make progress, given that public opinion polls show that more than 80 percent of the public believes smoking should be legal, we have a large, loyal and politically active customer base, and the industry has very strong legal positions. In the final analysis, it's in everyone's interest to come up with reasonable solutions that can resolve some of the controversy surrounding tobacco products. We're committed to doing so.

Meeting Commitments to Shareholders

Over the past year we've taken a number of steps to increase returns to shareholders, including a 23 percent increase in the common dividend and initiation of a share repurchase program, with \$100 million authorized and used in 1996. We see a number of opportunities to build on our successes this year and to find additional ways to improve returns for our shareholders. In the next few months we will examine both our dividend and repurchase programs to determine how much additional flexibility our improving

Exhibit Plf 17
Date 3/1?/97
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financial performance may provide us in 1997. Although the current environment makes an immediate spin-off of Nabisco to shareholders impractical, we remain committed to exploring spin-off options that will not damage either our food or tobacco businesses.

Finally, as part of our continuing effort to recruit additional, strong outside directors, the RJR Nabisco board recently elected H. Eugene Lockhart a director. Mr. Lockhart is president and chief executive officer of MasterCard International Incorporated, a worldwide company generating more than $500 billion in transaction volume through its 300 million MasterCard credit cards. His international experience and marketing background make him a welcome addition to the board.

Sincerely,

STEVEN F. GOLDSTONE
Chairman and Chief Executive Officer

R.J. Reynolds International
Performance Highlights

In the international tobacco business, net sales totaled $1.01 billion in the fourth quarter of 1996, a 19 percent increase over the 1995 quarter. Operating company contribution of $227 million rose by 10 percent. The improvement in sales and operating company contribution was driven by a 10 percent improvement in volume — three times the growth rate of the international tobacco industry's American-blend segment — improved product mix and pricing and increased marketing investment.

For the full year, international tobacco net sales grew 12 percent, while operating company contribution excluding one-time restructuring-related expenses and volume both increased by 10 percent.

Camel Lights, launched in more than 15 countries during 1996, grew volume substantially, helping to expand the company's participation in the "lights" segment and to grow volume and market share in Western Europe in 1996.

Winston's volume grew 12 percent during the year, reporting gains in Russia, France, Spain, Turkey and Greece as well as in a number of new markets.

This was an outstanding quarter for the company by virtually any measure.

Salem's 1996 growth was fueled by the performance of Salem Pianissimo — the advanced technology "less smoke, less smell" product in Japan — contributing to a 10 percent volume gain in Japan. At mid-1996, the company launched Premier Pianissimo in Japan, a non-menthol version of the Pianissimo product, and by year-end, the two Pianissimo products captured 1 percent of the Japanese market.

In the Former Soviet Union, core brands — Camel, Winston, Salem, Magna, North Star and Peter I — grew volume by more than 60 percent during the year, with each brand recording double-digit volume growth. Overall market share grew by two share points to almost 15 percent in 1996. In Central Europe, volume grew by 55 percent in 1996.

R.J. Reynolds Tobacco Company
Performance Highlights

The domestic tobacco business reported fourth quarter operating company contribution of $305 million, up 2 percent from the comparable quarter in the prior year. Domestic tobacco sales of $1.13 billion were stable, matching results in the 1995 fourth quarter.

The company's domestic volume declined 3 percent during the fourth quarter, as a result of heavy competitive promotional activity within the full-price segment and expected declines in Winston Select and the lower-margin savings segment.

For the full year, domestic tobacco operating company contribution of $1.45 billion was 2 percent higher than the $1.42 billion reported in 1995. Net sales totaled $4.55 billion, up 2 percent versus the prior year on a 4 percent volume decline.

In domestic markets, the Camel and Doral brands continued to post volume increases and retail share gains in the fourth quarter. R.J. Reynolds announced that the new Camel Menthol line, which was introduced into selected markets during the third quarter of 1996, is being expanded to national distribution in the first quarter of 1997. The Camel Menthol line extensions are designed to build on Camel's momentum and expand its marketplace opportunities.

DOMESTIC AND INTERNATIONAL FOOD AND TOBACCO BRANDS

DORAL
VANTAGE
More
NOW
Old Coast
GREY POUPON
PREMIUM

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Including Camel Menthol. Camel's shipments rose 7 percent in the quarter and were up 5 percent for the full year. Doral, the industry's leading savings brand, ad a 3 percent volume increase in the fourth quarter and grew 4 percent for all of 1996.

The company continues to monitor and evaluate the test market performance of several initiatives, including a new Winston positioning, the Red Kamel and Kamel Menthe line extensions and the innovative, reduced-smoke-technology Eclipse brands.

Nabisco

Performance Highlights

Nabisco's net sales for the fourth quarter were up 6 percent to $2.48 billion from $2.35 billion in 1995. Excluding one-time restructuring-related expenses, operating company contribution grew 19 percent to $408 million, from $344 million in the previous year.

For the full year, Nabisco's net sales of $8.89 billion in 1996 were up 7 percent from $8.29 billion recorded in 1995. Excluding one-time restructuring-related expenses, operating company contribution rose 9 percent to $1.23 billion from $1.13 billion in 1995.

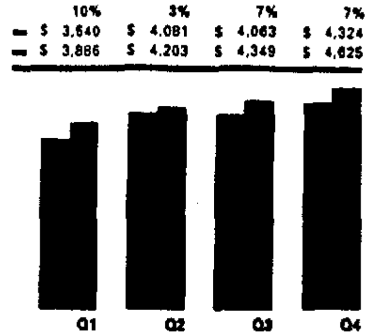
For the year, Nabisco reported improvement in its omestic business, with strong third and fourth quarter gains in the biscuit business, paced by the renewed momentum in core products — including Oreo, Ritz, Chips Ahoy! — and the highly successful new Air Crisps line. These gains were partially offset by ongoing softness in the biscuit wellness category.

Planters had a significantly better year than 1995, due to sales growth in the warehouse club and mass merchandising channels and a more stable competitive environment in the nut market.

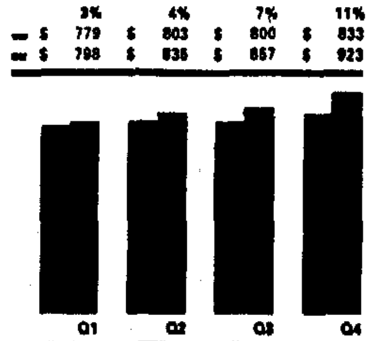
In the confectionery business, Life Savers continued to make gains during the year on the strength of the success of its new longer roll, expansion in the bagged candy category and the highly successful national introduction of Ice Breakers gum.

Another important driver in 1996 was Parkay margarine, acquired late in 1995, which fueled significant increases in the sales and earnings of the tablespreads business.

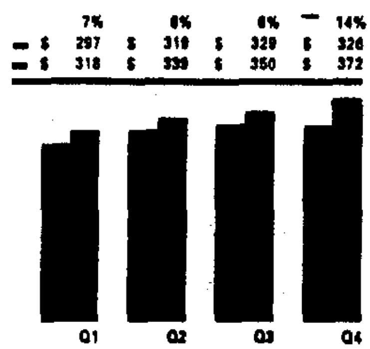
Nabisco International's profits softened, the result of higher commodity costs which could not fully recovered through pricing and of the slower-an-expected integration of several acquisitions which delayed full realization of operating efficiencies.



NET SALES
(% CHANGES VS. PRIOR YEAR)
$ IN MILLIONS
1995 ACTUAL
1996 ACTUAL



OPERATING COMPANY CONTRIBUTION*
(% CHANGES VS. PRIOR YEAR)
$ IN MILLIONS
1995 ACTUAL
1996 ACTUAL
*EXCLUDES CERTAIN ONE-TIME ITEMS



CASH NET INCOME AVAILABLE TO COMMON*
(% CHANGES VS. PRIOR YEAR)
$ IN MILLIONS
1995 ACTUAL
1996 ACTUAL
*EXCLUDES CERTAIN ONE-TIME ITEMS

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RJR Nabisco Financial Highlights

RJR Nabisco Holdings Corp.

Consolidated Condensed Statements of Income

(DOLLARS IN MILLIONS, EXCEPT PER SHARE AMOUNTS)

	THREE MONTHS ENDED DECEMBER 31, 1996	1995	TWELVE MONTHS ENDED DECEMBER 31, 1996	1995
Net Sales				
Total Tobacco	$ 2,142	$ 1,974	$ 8,174	$ 7,714
Total Food	2,483	2,350	8,889	8,294
Consolidated	$ 4,625	$ 4,324	$ 17,063	$ 16,008
Operating Company Contribution				
Total Tobacco (A)	$ 532	$ 418	$ 2,253	$ 2,063
Total Food (B)	338	344	1,130	1,129
Headquarters	(17)	(16)	(67)	(64)
Operating company contribution	853	746	3,316	3,128
Amorization of trademarks and goodwill	(161)	(159)	(636)	(636)
Restructuring expense (C)	–	(154)	(428)	(154)
Operating income	692	433	2,252	2,338
Interest and debt expense	(230)	(236)	(927)	(899)
Other income (expense), net (D)	(45)	(33)	(126)	(173)
ᶦncome before income taxes	417	164	1,199	1,266
⁄ision for income taxes	181	97	585	580
Income before minority interest in income of Nabisco	236	67	614	686
Less minority interest in income of Nabisco	21	23	3	59
Income before extraordinary item	215	44	611	627
Extraordinary item-loss on early extinguishments of debt, net of income taxes and minority interest	–	–	–	(16)
Net income	215	44	611	611
Less preferred stock dividends on a fully diluted basis	7	8	31	98
Net income applicable to common stock	$ 208	$ 36	$ 580	$ 513
Net income (loss) per common and common equivalent share on a fully diluted basis: (E)				
Income before extraordinary item	$ 0.63	$ 0.11	$ 1.76	$ 1.60
Extraordinary item	–	–	–	(0.05)
Net income	$ 0.63	$ 0.11	$ 1.76	$ 1.55
Average number of common and common equivalent shares outstanding on a fully diluted basis (in thousands)	329,069	330,505	329,832	329,828

(A) 1995 INCLUDES $87 MILLION ($59 MILLION AFTER TAX) OF COSTS AND EXPENSES INCURRED IN CONNECTION WITH THE CONSOLIDATION AND RELOCATION OF THE INTERNATIONAL TOBACCO OPERATIONS.

(B) 1996 INCLUDES NON-RECURRING RESTRUCTURING RELATED IMPLEMENTATION EXPENSES ASSOCIATED WITH THE FOOD BUSINESS OF $70 MILLION ($33 MILLION AFTER TAX, NET OF MINORITY INTEREST) FOR THE THREE MONTHS ENDED DECEMBER 31, 1996 AND $97 MILLION ($46 MILLION AFTER TAX, NET OF MINORITY INTEREST) FOR THE YEAR ENDED DECEMBER 31, 1996.

(C) 1996 INCLUDES A RESTRUCTURING EXPENSE OF $428 MILLION ($241 MILLION AFTER TAX, NET OF MINORITY INTEREST) INCURRED IN JUNE 1996 RELATED TO THE DOMESTIC AND INTERNATIONAL FOOD BUSINESSES OF $353 MILLION AND $75 MILLION, RESPECTIVELY. IN ADDITION, 1995 INCLUDES A RESTRUCTURING EXPENSE OF $154 MILLION ($104 MILLION AFTER TAX) RELATED TO THE DOMESTIC AND INTERNATIONAL TOBACCO BUSINESSES OF $100 MILLION AND $54 MILLION, RESPECTIVELY.

(D) 1995 INCLUDES $103 MILLION ($67 MILLION AFTER TAX) OF COSTS AND EXPENSES INCURRED IN CONNECTION WITH THE DEBT EXCHANGE OFFERS AND CONSENT SOLICITATIONS COMPLETED IN JUNE 1995.

ᶦCOME BEFORE EXTRAORDINARY ITEM PER COMMON AND COMMON EQUIVALENT SHARE ON A PRIMARY BASIS AMOUNTED TO $.65 AND $.10 FOR THE THREE MONTHS ENDED DECEMBER 31, ⁄96 AND 1995, RESPECTIVELY, AND $1.74 AND $1.58 FOR THE TWELVE MONTHS ENDED DECEMBER 31, 1996 AND 1995, RESPECTIVELY.

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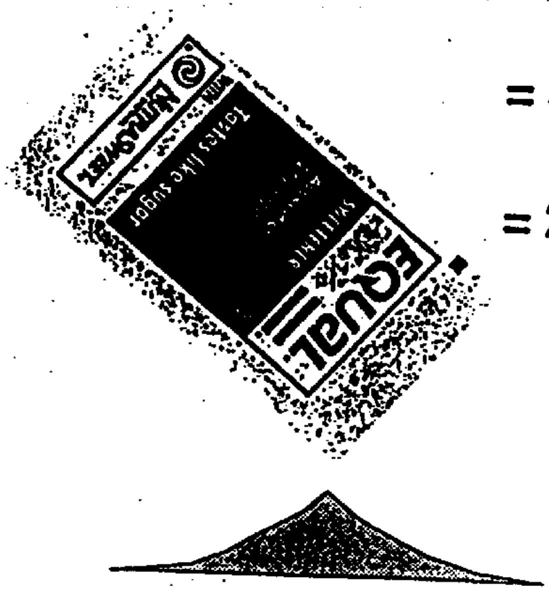
THE SMOKE FROM ONE 1992 WINSTON CIGARETTE CONTAINS APPROXIMATELY 10 NANOGRAMS OF BaP (0.000,000,010 grams)

MORE THAN 100,000,000 1992 WINSTON CIGARETTES WOULD BE REQUIRED TO PRODUCE ENOUGH BaP TO FILL A ONE GRAM PACKAGE OF EQUAL



= 50,000 Packs of 1992 Winston Cigarettes per year for 100 years

= 2 Packs per Day for more than 6,500 years

10233

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DOCUMENTATION OF THE THRESHOLD LIMIT VALUES AND BIOLOGICAL EXPOSURE INDICIES

Sixth Edition

1991

American Conference of Governmental Industrial Hygienists, Inc.
Cincinnati, Ohio

ISBN: 0-936712-96-1

Printed in the United States of America

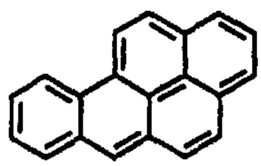
American Conference of Governmental Industrial Hygienists, Inc.
6500 Glenway Avenue, Bldg. D-7
Cincinnati, OH 45211-4438
U.S.A.

BENZO[a]PYRENE

CAS: 50-32-8

3,4-Benzpyrene; B[a]P

$C_{20}H_{12}$



TLV, None assigned

A2 — Suspected Human Carcinogen

1975: TLV, none, A2 — Suspected Human Carcinogen, proposed

1977–present: TLV, none, A2 Carcinogen

1991: Documentation written

Chemical and Physical Properties

Benzo[a]pyrene (B[a]P) is a polycyclic aromatic hydrocarbon (PAH) which exists in various crystalline forms when pure, usually as yellowish plates or needles.[1] Chemical and physical properties include:

- Molecular weight: 252.30
- Melting point: 179°–179.3°C
- Boiling point: 310°–312°C
- Density: 1.351
- Solubility: insoluble in water; soluble in benzene, toluene, and xylene; sparingly soluble in ethanol and methanol

Major Uses or Sources of Occupational Exposure

In nature, B[a]P is considered an environmental pollutant, usually bound to small particulate matter present in urban air, industrial and natural combustion emissions, and cigarette smoke. Although epidemiological and toxicological studies have confirmed that B[a]P is a potent carcinogen, B[a]P emissions are not controlled in the United States. Furthermore, no environmental standards for safe levels of exposure to humans have been established.

At least 1000 tons of B[a]P are produced every year in the U.S.,[2–4] the majority of which is produced by coal heating furnaces, refuse burning, and industrial plants (B[a]P emission sources are reviewed extensively by Griciute.[5]) B[a]P is found in the environment, and its levels are often used as a rough index of air pollution and of total PAHs. Humans are exposed to PAHs in air, water, and food. Baum[3] estimated human B[a]P exposure to be about 100 ng/m^3 in heavily polluted air, 23 ng/L in drinking water, and up to 100 μg/kg in smoked foods. The validity of these data to predict present day levels is questionable, however, because B[a]P is released predominantly in the vapor state and is minimally detected by conventional sampling methods used in industry.[5] Furthermore, Perera[6] noted the greater reliance of industry on coal and synfuels since the time the Baum data were obtained, and these estimates grossly underestimate the amount of B[a]P currently released into the atmosphere.

Upon combustion, more than 75% of the B[a]P produced is found concentrated in submicron particles (< 2.3 μm) that easily penetrate the lower lung and alveoli.[7] Once deposited in the lung, B[a]P is readily eluted into surrounding tissues where it can be activated to one of many carcinogenic forms, capable of tumor initiation.[8] Within the lung, B[a]P clearance is inefficient, ranging from days to years, and is markedly impaired by cigarette smoking.[8]

Animal Studies

Carcinogenicity

A great amount of literature exists which conclusively demonstrates the carcinogenicity of B[a]P. In all animal species tested to date (mouse, rat, hamster, rabbit, guinea pig, duck, newt, dog, monkey) and in fish,[9–11] B[a]P has proven *carcinogenic*. B[a]P acts *locally*, as evidenced by tumor development at the site of administration. B[a]P also acts systemically, however, an action best evidenced by pulmonary adenomas in mice resulting from any route of administration.[6] Because B[a]P is a procarcinogen, potency is directly dependent upon the levels of activation enzymes (i.e., P-450s, sulfotransferases); therefore, carcinogenic potency is exceptionally species- and condition-specific. Table 1 is a summary of tumor production in both rats and hamsters exposed to B[a]P at different doses, routes of administration, and adsorbents. These two species were chosen as the focus for this review because: 1) data including broad dose ranges could be obtained in these species so that low-level exposures could be used to predict potential threshold doses and 2) the Syrian golden hamster is the model that most closely reproduces the morphology of human respiratory cancers.[12]

Three very important trends are evident upon examination of Table 1. First, a dose–response relationship was established in all studies, and in many cases where a broad range of dosages was tested, the dose–response curves extrapolated to zero. This suggests that no threshold dose exists upon administering B[a]P *in vivo* in these species. Complete absence of tumors was only evident when B[a]P was administered at 0.1 mg (total dose) in rats, and this was not the case in all studies. For example, Yanisheva[13] did not observe any tumor development in rats when 0.1 mg B[a]P was injected intratracheally; whereas in other experiments,[14] tumors

were induced by administering the same total dose in smaller aliquots by the same route. These data illustrate another trend evident in Table 1; repeated administrations of B[a]P appeared more potent at initiating tumors than a single dose of the same amount. Furthermore, the latency period for tumor development in rats is shorter upon administration of increasing amounts of B[a]P, and tumor type (e.g., epithelial tumors of the lungs or lung reticulosarcomas) also change with different single doses of B[a]P.[14] Similar effects were observed in hamsters.[17] Finally, other pollutants that are found in significant amounts with B[a]P can act synergistically in tumor production as evidenced in rats exposed to similar amounts of B[a]P with varying sulfur dioxide concentrations.[15]

Because low-level risk assessment for B[a]P is difficult using animal carcinogenicity data obtained at high doses, models designed to predict carcinogenicity at low doses using either DNA or protein adduct formation have been developed.[4,19] These studies have trends similar to those seen with *in vivo* models (Table 2). For example, a linear dose–response curve which extrapolates to zero is obtained upon oral administration of 2–1351 μmol/kg B[a]P to mice.[4] Again, no threshold dose is obtained, even when administered doses are at or below the level of normal human exposure (0.2–1.6 μg daily).

Dunn[19] has shown that adduct formation and tumorigenesis correlate well in mice as evidenced by parallel dose–response curves. Furthermore, because turnover of DNA adducts was the same at all doses, Dunn stated that "interactions between DNA and ingested benzo[a]pyrene takes place in the same manner both at high doses typical of laboratory carcinogenesis experiments and at low doses typical of human exposure."

TABLE 1. Tumorigenic Responses to Benzo[a]pyrene Exposure

Animal	Dose	Response	Comment	Reference
Rat	Subcutaneous injection of B[a]P in olive oil		Dose–response relationship observed, even at low doses. No threshold observed.	12
	0.05 mg	1 tumor/7 animals		
	0.1 mg	4 tumors/31 animals		
	0.5 mg	9 tumors/17 animals		
	1.0 mg	84 tumors/60 animals		
Rat	Intratracheal B[a]P given in 10 doses Total dose	% malignant bronchiogenic tumors	No tumors observed at 0.1 mg B[a]P.	13
	0.1 mg	0%		
	0.5 mg	15%		
	2.5 mg	30.7%		
	25 mg	42%		
Rat	Tenfold intratracheal administration of 0.1 mg total		Similar experiment as above shows significant response at 0.1 mg. Method of dosing and type of response important.	14
	1 administration	No tumors		
	5 administrations	No tumors		
	10 administrations	Tumors at 25 months		
Rat	Tenfold intratracheal administration giving total dose		Latency period shortened when B[a]P dose is increased. Doses over 10 weeks, not animal's lifetime.	14
	0.005 mg	No tumors		
	0.02 mg	No tumors		
	0.1 mg	Tumors at 27 months		
	0.5 mg	Tumors at 19 months		
	2.5 mg	Tumors at 17 months		
	25.0 mg	Tumors at 13 months		
Rat	10 mg/m^3 B[a]P via inhalation + increasing [SO_2]	Squamous cell carcinomas increase with increasing [SO_2]	Synergistic activity of two pollutants given concurrently.	15
Rat	Injection of 3 mg B[a]P into hind leg	Local tumors in area of application of all animals	Shows that B[a]P acts locally.	16
Hamsters	37.5 B[a]P + 12.5 mg ferric oxide	18% respiratory tract tumors	Single, large dose of B[a]P required to show distinct tumor response.	17
	5.0 mg B[a]P + 45 mg ferric oxide	4% respiratory tract tumors		
Hamsters	Total dose of 3 mg B[a]P + 3 mg ferric oxide given in 5, 10, and 15 administrations	Linear dose–response curves with increased potency with smaller administration increments	Higher tumor probability and shorter latency period when given 15X > 10X > 5X	17

TABLE 2. DNA Adduct Formation Upon Exposure to Benzo[a]pyrene

Test System	Dose	Comments	Reference
Salmonella typhimurium strain TA98	As little as 0.5 µg/plate gave significantly higher revertant rate than controls.	One of many studies showing mutagenicity in Ames assay.	2
Mice	P.O. administration of 2–1351 µmol/kg.	B[a]P metabolite/DNA adduct formation in liver, lung, and forestomach.	4
Mice	Single P.O. dose of 1 µg B[a]P/mouse.	Adduct formation highest in liver > intestine > colon > stomach.	19
Mice	50–1600 nmol B[a]P applied topically.	Tumorigenicity at 24 weeks and B[a]P adduct formation gave parallel dose-response curves. Smallest dose (50 nm) gave papillomas suggesting no threshold.	20
Human, monkey, dog, hamster, rat	1 µM B[a]P incubation for 24 hours in cultured bladder and tracheobronchial explants.	pmoles metabolite/mg DNA: human, 1515 ± 875; hamster, 364 ± 170; dog, 296 ± 291; monkey, ND; rat, 14.9 ± 11.7	21
Human hepatocytes	Exposed 24 hours to 0.1–100 µM B[a]P.	Linear binding to DNA from 0.1–10 µM; however, up to 800-fold increase at 100 µM, so cannot extrapolate from high concentrations.	22
Mice	Oral administration of B[a]P at 120 mg/kg/day between gestational days 2 and 10.	Teratogenic increased intrauterine toxicity and malformations in susceptible strains as compared to nonsusceptible strains.	23

Although absolute organ specificity of B[a]P has not been demonstrated, mice exposed to a single dose of B[a]P orally had more prevalent DNA adducts in the liver than in the intestine, colon, and stomach. This demonstrates that B[a]P does not always act locally. In rats, B[a]P adduct formation and metabolism are greatest in the liver,[24] although no studies were found in which B[a]P exhibited hepatocarcinogenicity. B[a]P carcinogenicity is species specific; however, specificity has been attributed to the relative persistence of DNA adducts, suggesting that DNA repair plays a very important role in protection against B[a]P carcinogenicity *in vivo*.[25]

Reproductive/Developmental

B[a]P affects both male and female reproductive capacity and has been shown to cause gonadal dysplasia and reduced fertility in both sexes of mice.[26] When administered at high doses early in gestation, B[a]P elicits intrauterine toxicity and teratogenicity (Table 2).[23]

Pharmacokinetic/Metabolism Studies

B[a]P uptake by cells is receptor-mediated, and transport to intracellular sites of metabolism is thought to be protein-mediated. Soues et al.[27] have identified hepatic lipoproteins capable of intracellular transport of B[a]P. Similarly, a protein involved in transfer of B[a]P to sites of metabolism and capable of facilitating release of oxidized products has been isolated.[28] Microsomal metabolism of B[a]P produces many oxidized products capable of binding to DNA and proteins. For example, the formation of 7,8-dihydroxy-9,10-epoxy-7,8,9,10-tetrahydrobenzo[a]pyrene, the most potent carcinogenic metabolite of B[a]P, occurs by primary oxidation via the cytochrome P-450 system, hydrolysis of this oxidized metabolite by epoxide hydrase, and further epoxidation by the P-450 monooxygenase system. This ultimate carcinogen binds predominantly to the exocyclic 2 amino position of guanine bases to form a stable covalent adduct.[4-6,29] The exact mechanism by which B[a]P causes a mutation or initiates carcinogenesis is not known, but either could result from a transversion mutation by base mispairing or a frameshift mutation as is seen in viruses. It should be noted that the cytochrome P-450 system is not the only intracellular enzyme system capable of B[a]P metabolism. Recent evidence suggests that metabolites other than dihydrodiolepoxides are produced *in vivo* in significant amounts that can elicit carcinogenic activity. For example, Surh et al.[30] have demonstrated cytosolic conjugates of B[a]P involving 3′-phosphoadenosine-5′-phosphosulfate (PAPS) that form reactive sulfuric acid esters able to form benzylic adducts with deoxypurine nucleotides. In addition, glutathione and UDP glucuronate conjugating enzymes participate in the metabolic fate of B[a]P within cells.[31]

Much work has been done to identify the toxic metabolites of B[a]P, but much more remains to be done to ascertain their pertinence to human risk assessment. Hamster and mouse liver microsomal metabolism of B[a]P produces different products from those observed

TABLE 3. B[a]P Dose–Response Estimates Derived from General Air Pollution Epidemiology

Estimate	Assumptions or Comment	Reference
Investigators reported approximately doubling of lung cancer mortality in large cities, with intermediate rates in surburban areas.	Similar results obtained in four studies. Difference cannot be explained by smoking differences between area studies.	34
Increase of 1 μg B[a]P per 1000 m^3 of air was related to 5% increase in pulmonary cancer death rate.	Author concludes that 60% reduction in air pollution might reduce pulmonary deaths 20%.	13
Increases in lung cancer death rate in smokers per B[a]P "unit" range from 10% (light), 5.5% (moderate), to 1.1% (heavy) and 13% (nonsmokers). For moderate smokers, a "unit" B[a]P was associated with an excess $104/10^5$ lung cancer deaths.	A unit B[a]P is defined here as 7.0 ng/m^3 B[a]P; therefore, an excess 14.5 deaths/100,000 would be associated with 1 ng/m^3 B[a]P. Average increase per ng/m^3 B[a]P in smokers is 5.8%.	6
$1.4/10^5$ and $0.4/10^5$ extra deaths are attributable to 1 ng/m^3 B[a]P in smokers and nonsmokers, respectively.	Results for nonsmokers are remarkably consistent with those derived from British gas workers' data; differences in duration of exposure might explain 3–4 times higher results obtained here for smokers in general population compared with smokers among gas workers.	6
A 4% increase in the lung cancer death rate in smokers is associated with 1 ng/m^3 B[a]P.	Hitosugi recorded an average 60% increase in lung cancer mortality for smokers (120% for light smokers) in areas of high B[a]P; the difference in annual average B[a]P levels in high vs. low pollution areas was 16 ng/m^3 (estimated as 30% of yearly maximum). (For light smokers taken as a separate class, a 7.5% increase in lung cancer mortality was associated with a 1 ng/m^3 increase.)	6

in the rat.(32) Furthermore, incubation of B[a]P with intact hamster embryo cells showed a markedly different metabolite profile than that observed with either hamster tissue microsomes or disrupted hamster cells. Therefore, whether these studies accurately represent the biochemistry of B[a]P within humans is questionable, so risk assessment based upon animal model studies must proceed with caution.

B[a]P metabolites have been shown to bind to DNA in cultured human hepatocytes,(22) as well as in human bladder and tracheobronchial explants.(21) The metabolites identified in the latter study were identical to those produced in other species and only differed in the relative percentages of formation. In fact, human tissues are most active in metabolizing B[a]P, exhibiting at least a threefold higher covalent binding to DNA than hamsters, dogs, monkeys, or rats. Therefore, the data in Table 2 suggest that humans possess all properties of B[a]P metabolism to make them as susceptible as animals (if not more) to the various exposures of B[a]P experimentally and that animal data should be considered, albeit cautiously, in assessing safe levels of exposure to B[a]P in the environment and workplace.

Human Studies

The primary route of B[a]P exposure is via inhalation, and the majority of epidemiologic studies to date have studied the correlation between mortality from lung cancer and B[a]P exposure. Although cigarette smoking, air pollution, and occupational exposure are all significant means of inhalation exposure, it is generally agreed that cigarette smoking is the overwhelming factor in the causation of lung cancer (reviewed by Carnow(33)). Although the chronic effects of lung cancer are of greatest concern, skin cancer, dermatitis, photoallergy,(7) non-neoplastic

TABLE 4A. B[a]P Dose–Response Estimate Derived from Occupational Epidemiology

Estimate	Assumptions or Comment	Reference
Extrapolation from observed excess $160/10^5$ lung cancer cases in British gas workers from exposure to the equivalent of 440 ng/m^3 B[a]P in general air pollution gives an estimated $0.4/10^5$ extra lung cancer cases/year per ng/m^3 B[a]P in the general population.	Workers were exposed to 1000 ng/m^3 B[a]P for about 22% of the year (assuming 40-hour workweek with 3 weeks annual leave); therefore, exposure was 2000 x 0.22 or 440 ng/m^3 B[a]P.	6
Reviewed literature on lung cancer death rates among U.S. coke oven workers and found a doubling or 10-fold excess in lung cancer death rate vs. unexposed controls.	Estimated exposure was 2000 ng/m^3 B[a]P when at work.	33
Concluded that an increase of 2.5% in expected lung cancer deaths per ng/m^3 exposure increase in B[a]P.	Author assumed that workers were exposed to 1200 ng/m^3 for 24% of total time (in years).	33

TABLE 4B. B[a]P–DNA Adducts in Humans by Immunoassay (polyclonal)*

Studied Populations	Tissue	No. Positive
Roofers	Lymphocytes	7/28
Foundry workers	Lymphocytes	7/20
Smokers/nonsmokers	Lung tissue	7/23
Volunteers	Peripheral alveolar macrophages	3/5
Lung cancer patients	Lung tissue	4/14
Lung cancer control subjects	Lung tissue	0/13

*From Perera et al.[34]

respiratory disease, and emphysema[33] have all been implicated from various routes of B[a]P exposure.

Tables 3–5 summarize epidemiologic studies from a variety of B[a]P exposure sources, most of which have been reviewed by Perera.[6] There is a significant correlation between B[a]P and lung cancer mortality. These data assume that exposure indices and B[a]P levels are linearly related, which is probably a valid assumption when B[a]P levels are used as an assay for indexing air pollution. Interestingly, Carnow[33] (Table 4) has noted in his studies that lung cancer rates were not the highest in the most urbanized areas; rather, lung cancer was most prevalent in areas that had the highest B[a]P levels. Furthermore, levels of gross particulate matter were measured in these studies and they did not correlate with lung cancer morbidity. Collectively, these data suggest that B[a]P is a significant causative agent of lung cancer in epidemiologic studies involving air pollution, but B[a]P may not be present in levels directly proportional to total air pollution levels. Epidemiologic data pertaining to workers exposed to diesel emissions (Table 5) show no positive correlation with lung cancer morbidity; however, these studies are inconclusive because they do not allow for the latency period necessary to measure lung cancer incidence accurately.[6] This latency period could be as long as 30 years, and its peak incidence occurs after the age of 50.[35]

A comprehensive toxicological profile for B[a]P was published in 1990 by the U.S. Agency for Toxic Substances and Disease Registry (ATSDR).[36]

TLV Recommendation

The results of the epidemiologic and animal studies indicate the need for the establishment of rigorous control standards for B[a]P. Although epidemiologic data are not quantitative in nature, it is obvious that increased exposure to B[a]P is hazardous. It can be seen from these data that as little as 0.05 mg of B[a]P can initiate tumors in experimental animals and that 0.1 μM (25 μg/L) B[a]P is toxic to cultured human hepatocytes. It has been estimated that millions of people living near coke ovens are exposed to 100 μg B[a]P daily. Because small, repeated doses of B[a]P are more effective at tumor initiation than single administrations and because these people are probably exposed to other synergistically acting pollutants, they are exceeding safe exposure levels. Maximum allowable concentrations for B[a]P have been proposed by Shabad,[37] and these are the current limits legislatively imposed in the USSR: 0.1 μg/100 m^3 in ambient air and 15 μg/100 m^3 in air of workplaces. These concentrations are not considered to be safe; rather, they can be interpreted as "unavoidable doses." Presently, ambient concentrations of B[a]P significantly exceed the USSR maximum exposure level;[6] without

TABLE 5. Summary of Epidemiological Studies of Workers Exposed to Diesel Emissions*

Effect and Population Studied	Exposure Classification	Results	Caveats
Mortality and morbidity in London Transport staff exposed to diesel; men aged 45–64 were studied from 1950 to 1964.	Men were grouped in order of estimated exposure to exhaust fumes based on general observation and not chemical estimation.	A total of 96 deaths were from lung cancer, ill-health retirements, and transfers due to lung cancer; highest rate was in 2nd least exposed group (trolley-bus engineering staff); no excess was found in highly exposed group; association was found with place of residence.	The number of cases was very small; the study did not take into account the long latency period of lung cancer; smoking histories were not taken.
Mortality in U.S. railway workers; 151 deaths between 1953 and 1958 due to cancer of lung and/or bronchus were studied.	Workers were divided into 3 groups based on estimated exposure.	The least exposed group had the highest lung cancer mortality; an association was found with residence in urban areas.	Selection in retiring ill employees was not evaluated; smoking was not considered; other causes of death that compete with lung cancer were not evaluated; small number of deaths.
Mortality in potash workers from 8 mines (2 dieselized) was studied for the period 1940–1967.	Workers in dieselized mine were compared with nondieselized.	No excess mortality from lung cancer was found in exposed workers.	Mines dieselized only since 1949 and 1957 (insufficient time for induction?); small number of deaths (31) may preclude significant results.

*From Perera.[6]

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regulation, there is no incentive for industry to control PAH emissions. Based on the positive results in animal carcinogenicity studies and the significant correlation between B[a]P exposure and lung cancer in limited studies, the TLV Committee has designated B[a]P as an A2 carcinogen, suspected human carcinogen, without an assigned TLV.

Other Recommendations

OSHA PEL: OSHA has established a PEL–TWA of 0.2 mg/m^3 for B[a]P (a coal tar pitch volatile as described in 29 CFR 1910.1002).[38,39] B[a]P (coal tar pitch volatiles) is one of the 160 substances for which the PEL was unchanged and was not evaluated during the 1989 OSHA rulemaking on air contaminants — permissible exposure limits.

NIOSH REL/IDLH: NIOSH considers B[a]P (in the cyclohexane extractable fraction of coal tar products) to be a potential human carcinogen and recommends a REL–TWA of 0.1 mg/m^3.[40] NIOSH established an IDLH value of 700 mg/m^3 [CARCINOGEN] for coal tar pitch volatiles.

ACGIH Rationale for TLVs that Differ from the PEL or REL: B[a]P is grouped by OSHA and NIOSH with those substances identified as either coal tar pitch volatiles, benzene-soluble fraction (OSHA), or coal tar products, cyclohexane-extractable fraction (NIOSH), and for which a generic PEL or REL has been promulgated or recommended. The recommendation by the TLV Committee of an A2 suspected human carcinogen designation for B[a]P, without a TLV, and listing it as a separate chemical substance is based on the Committee's recognition of B[a]P as a ubiquitous environmental pollutant arising from industrial and natural combustion emissions; the unequivocal demonstration of B[a]P as an animal carcinogen with no threshold dose identified, even at this time; and the correlation between B[a]P and human lung cancer.

NTP Studies: NTP has completed intratracheal, inhalation, and immunotoxicology studies of B[a]P. Results have not been reported. B[a]P was positive in the *Salmonella*, mouse lymphoma, and chromosome aberrations/sister-chromatid exchange assays and negative in *Drosophila* sex-linked recessive lethal/reciprocal translocation tests.

Carcinogenic Classification

IARC: Group 2A, probably carcinogenic to humans.

MAK: Group A2, unmistakably carcinogenic in animal experimentation only.

NIOSH: Carcinogen, with no further classification.

NTP: Group 2, reasonably anticipated to be a carcinogen.

TLV: A2, suspected human carcinogen.

Other Nations

Australia: Category 2, probable human carcinogen (1990); Federal Republic of Germany: no MAK, Group A2, unmistakably carcinogenic in animal experimentation only; technical guiding concentrations (TRK), production, loading and unloading of pencil pitch, near the ovens in coke plants 0.005 mg/m^3, others 0.002 mg/m^3 (1990); Sweden: 0.005 mg/m^3, short-term value 0.03 mg/m^3, 15 minutes, skin, carcinogen (1984); United Kingdom: coal tar pitch volatiles (as cyclohexane solubles) 0.14 mg/m^3, carcinogen (1991).

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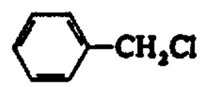
BENZYL CHLORIDE

CAS: 100-44-7

α-Chlorotoluene

C_7H_7Cl



TLV–TWA, 1 ppm (5.2 mg/m^3)

1954: TLV–TWA, 1 ppm, proposed

1956–present: TLV–TWA, 1 ppm

1991: Documentation revised

Chemical and Physical Properties

Benzyl chloride is a colorless, refractive liquid with a pungent odor. The stabilized form of benzyl chloride contains a fixed amount of a sodium carbonate solution or propylene oxide. Chemical and physical properties include:

- Molecular weight: 126.58
- Specific gravity: 1.100 at 20°C
- Boiling point: 179°C
- Freezing point: –39°C
- Vapor pressure: 1.0 torr at 22°C
- Flash points: 67°C, closed cup; 74°C, open cup
- Lower explosion limit: 1.1% by volume in air
- Autoignition temperature: 525°C
- Solubility: insoluble in water; miscible with most organic solvents
- Reactivity: very reactive; unless stabilized, it undergoes a Friedel–Crafts-type condensation when exposed to certain metals, liberating hydrogen chloride

Major Uses or Sources of Occupational Exposure

Benzyl chloride is a chemical intermediate in the manufacture of dyes, plasticizers, lubricants, gasoline additives, pharmaceuticals, tanning agents, and quaternary ammonium compounds.

Animal Studies

Acute

Two-hour LC_{50} values of 80 ppm and 150 ppm benzyl chloride are cited for the mouse and rat, respectively.[1] Back et al.[2] reported that all mice and rats survived a 1-hour exposure at 400 ppm. The difference in the results of these two studies cannot be explained. Rabbits and cats exposed 8 hours/day for 6 days at 95 ppm showed eye and respiratory tract irritation, while a dog died following 8 hours at 380 ppm.[3] Skin sensitization in guinea pigs has been reported.[4]

Chronic/Carcinogenicity

Weekly, subcutaneous, high dose (80 mg/kg) administration of benzyl chloride for 51 weeks resulted in injection site sarcomas, with lung metastases, in rats; the mean induction time was 500 days. At half this dosage, there were some local sarcomas but no metastases.[3,5] The National Institute for Occupational Safety and Health (NIOSH) concluded that the presently available data are insufficient upon which to base a firm conclusion as to the carcinogenic potential of benzyl chloride.[3]

In a study by Lijinsky,[6] benzyl chloride was administered by gavage in corn oil at a dose of 50 or 100 mg/kg body weight (mice) and 15 or 30 mg/kg (rats) 3 times/week for 2 years. A statistically significant increased incidence of papillomas and carcinomas of the forestomach was observed in mice of each sex. The only statistically significant increased incidence of neoplasms in the rats (female only) was for thyroid C-cell tumors. A few neoplasms of the forestomach were observed in male rats. Based on the subcutaneous and gavage studies, benzyl chloride was evaluated by the International Agency for Research on Cancer (IARC)[7] to have limited evidence for carcinogenicity in animals.

Genotoxicity Studies

The IARC review of benzyl chloride[7] reported that the substance did not induce micronuclei in mice treated *in vivo*. It induced DNA strand breaks, but not unscheduled DNA synthesis or chromosomal aberrations in cultured human cells. Conflicting results were obtained for the induction of sister-chromatid exchanges in human cells. In cultured rodent cells, benzyl chloride induced sister-chromatid exchanges, chromosomal aberrations, mutation and DNA strand breaks. It induced somatic and sex-linked recessive lethal mutations in Drosophila; mitotic recombination, gene conversion, mutation and DNA damage in fungi; and mutation and DNA damage in bacteria.[7]

Human Studies

According to Smyth,[8] "This [benzyl chloride] is a potent lacrimator irritating to the eye, nose, and throat and capable of causing lung edema. . . . It may be inferred that the liquid causes corneal injury. . . . The 1 ppm threshold limit can be derived from older human sensory data. It is undoubtedly low enough to prevent lung injury."

From references cited in the NIOSH criteria document for benzyl chloride,[3] exposure at 1.5 ppm for 5 minutes can result in slight conjunctivitis, and 8 ppm is the eye irritation threshold for a 10-second exposure. A single breath of air containing 35 ppm of benzyl chloride will reportedly cause nasal irritation. Flury and Zernik[9] reported that a 1-minute exposure at 16 ppm was intol-

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sta; D. Hoffmann.
aVoie; F. Bock; G. Gori.
:. Tso; P. Asmus.

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Banbury Report

CSH

A SAFE CIGARETTE?

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Exhibit
Date 5/29/97
A.W.R. & Assoc.

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SESSION 3: Discussion

Monday Evening
October 15, 1979

Risk-Reduction Achievements and Future Directions

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McELHENY: We obviously have been talking all day about the degree to which smoking risks have already been reduced. To lead tonight's discussion we have enlisted Michael Russell who has placed major questions for discussion on the blackboard:

1. Have the risks of lung cancer been reduced for people who continue to smoke cigarettes?
2. If so, is this reduction due to changes that have occurred in cigarettes, or is it due to changes in smoking habits, or to other things? In other words, are cigarettes less hazardous today than they were 20 years ago?
3. If cigarettes are now less hazardous with regard to their carcinogenic effect, how much of this is due to changes in the quantity as opposed to the quality of the tar they produce?

RUSSELL: I must say I've found it a pretty baffling day hearing expert epidemiologists and then experts in the biological fields. I think we should try to answer these three questions from epidemiological evidence and see how far we get; then we can look at how the epidemiological data link up with biological and smoking-machine data.

So, are the epidemiologists able to say "yes" to the first question? Have the risks of lung cancer been reduced for cigarette smokers?

GORI: Perhaps you'd like to start with England, where the evidence is more clear than in other countries.

RUSSELL: Since I'm not an epidemiologist I don't wish to answer the question myself.

SHIFFMAN: You might also want to open discussion to the cardiovascular diseases. We've repeatedly pointed out that, at least in the United States, these are a more frequent cause of death.

RUSSELL: That's a more difficult area—let's take one thing at a time.

SCHWARTZ: It's been stated often that the cardiovascular disease mortality rate has declined in the U.S. This rate decline has been used politically on a number of occasions in the last year. But it appears that the so-called decline had occurred before any effective intervention or change in smoking or dietary habits had occurred.

It's important to note that a number of diseases appear to show a cyclical frequency over time in a society. We may be observing a spontaneous change in the frequency or severity of cardiovascular disease—coronary disease in particular—that has had nothing to do with any intervention or change in social habits. I don't think that we have any evidence of a significant change in cardiovascular disease in this country that would not have occurred spontaneously.

GORI: When you say "spontaneously," what do you mean? What is natural?

SCHWARTZ: By "spontaneous change" I mean something that we didn't do something to. A number of diseases like tuberculosis have periods where they're frequent and periods where they're less frequent in society. This phenomenon is partly explicable. But, in fact, the decline in cardiovascular disease mortality started before there was any significant change in diet, cholesterol, etc.

KEITH: But you are forgetting there have been a lot of changes in cigarettes over the last 20–25 years. I don't know whether that has correlated with any decrease in disease or not.

RUSSELL: Let's just deal with lung cancer first, then we can deal with coronary artery disease.

GORI: I would agree with that because with the coronary problem there are so many other risk factors to be considered.

RUSSELL: We have talked about cancer quite a lot today and seen some fascinating data. Would anyone like to say unequivocally "yes" or "no" to the first question?

WYNDER: That was my talk this morning (Wynder, this volume), and I think the data speak for themselves. We have presented two sets of data. The retrospective study from our group included more than 1000 cases of lung and larynx cancer and showed a reduction in risks among long-term filter cigarette smokers of 10 years or more of between 25% and 33% for both men and women (Wynder and Stellman 1979). This finding has been confirmed by the prospective studies of the American Cancer Society (Hammond et al. 1976). Furthermore, these appear logical, namely since lung cancer risk is known to be dose-related, a reduction in risk would be expected with a reduction in tar yields.

In our own studies and in the prospective studies, the 33% reduction in risk for filter cigarette smokers is in comparison to smokers of nonfilter

cigarettes—cigarettes that have also changed over the last 30 years. In other words, today's unfiltered cigarette has approximately 27 mg tar, whereas an unfiltered cigarette of 20 years ago had 40 mg tar.

RUSSELL: Does anyone want to argue or say that that's not so?

HARRIS: What would Dr. Wynder say about the changing cell type in lung cancer, from the squamous cell carcinoma to adenocarcinoma, and the increased incidence of peripheral carcinoma? Also, how would he relate those established facts, or perhaps not-established facts, to the general premise that the risk of cancer will continue to be reduced?

WYNDER: The important shift in work coming out of Roswell Park Memorial Institute on glandular and squamous lung cancer (Vincent et al. 1977) was somewhat puzzling to me. We have not been observing this at Sloan-Kettering Memorial, and I have suggested for some time that we ought to get the pathologists together to determine whether indeed they interpret slides in the same way in different hospitals. You'll find that most lung cancers will have a segment of both squamous and adenocarcinoma mixed. Before I could really answer whether there has been, in fact, an increase in glandular lung cancer, I want to make sure that we have a total agreement of pathologists. But it is intriguing for the larger question, which we need to follow up.

RUSSELL: I think now we can go on to the second question: "Is this reduction due to changes that have occurred in cigarettes, or is it due to changing smoking habits, or other things?"

GORI: There is one aspect of this change that we need to keep in mind. When you take the age-specific rates of lung cancer mortality trends, you begin to see a downward trend in the lower age groups, a flattening out at about 50, and an increase in higher age groups. These differences, in my opinion, reflect the previous smoking experiences of the various age groups concerned. Younger people have been smoking the lighter cigarettes for most of their careers. Older groups started their smoking period on the stronger cigarettes and they probably still continue on these. I think this aspect may shed some light on your second question.

McELHENY: Gio, is this American data or English data?

GORI: American data.

HARRIS: These are age-specific death rates of the entire American population, not the death rates of smokers.

GORI: That's correct.

HARRIS: If you were to look at the most recent birth cohorts, you would find that the peak prevalence of smoking, among males in any case, has declined over

time. The 30- and 35-year olds are not primarily those who smoke filter cigarettes or less toxic cigarettes, but they're people who have not smoked at all. The lung cancer rates are down because a greater percentage have not smoked at all.

GORI: Well, obviously, if you have a decline in incidence of lung cancer among smokers, the proportion of nonsmokers that get lung cancer is going to increase. But the total figure is going down.

WYNDER: I'd like to add a little perspective to the discussion, by telling you that the unique feature that most people do not fully recognize about lung cancer is that among 100 patients with Kreyberg type-I cancer, there would probably be no more than one nonsmoker.

RUSSELL: We're not arguing at this stage whether it causes cancer. We probably agree with you there. I'm just asking whether the reduction in the risk to smokers can be attributed to the changes that have occurred in cigarettes over the past 20 years.

McELHENY: Could you argue that the Austrian study (that shows no change in some of these lower age cohorts) would incline you to answer "yes" to question 2, since the Austrians seem to continue to smoke a cigarette that is higher in tar than is found on the average in other countries (Kunze, this volume)? Wouldn't that be a piece of evidence in support of a "yes" answer to question 2? Are there any other studies that would do the same thing, or am I torturing the data?

WYNDER: Another very important change in the epidemiology of lung cancer is that, to use a British term, lung cancer is becoming a disease of social class five. We have such a social class in this country, and our studies are showing that lung cancer is increasingly becoming a disease of the blue-collar worker. This again is a reflection of the fact that the upper-income groups are either quitting the habit or smoking cigarettes with the lower tar yields.

GORI: Another element of information to consider is the general levels of air pollution in the country. Most of the evidence that we have indicates no great relationship between air pollution and lung cancer incidence. At least up to now smoking has had the prevalent effect on the incidence of lung cancer. Things may change, of course, if the smoking effects are decreasing.

RUSSELL: Let's just say then that there's a reduction in incidence of lung cancer. That doesn't answer question 2, because that reduction could be due to people giving up cigarettes, rather than to some improvement in the risk of people who don't give up smoking. Quite frankly, I don't see how you can go on to answer question 3 unless you can prove question 2.

GORI: We proved 2 by showing that one particular type of cigarette, when compared to another type of cigarette, can be associated with lower risk.

RUSSELL: That's the first bit of relevant information we've had. Dr. Wynder started telling us how he'd seen so many smokers who had lung cancer and hardly any nonsmokers. That's irrelevant to question 2. Now you've given us the first bit of relevant evidence, which is a difference in lung cancer risk in smokers of different kinds of cigarettes. Now, does that evidence answer it, because those are self-selected samples.

Ernst Wynder has claimed that filter-tipped cigarette smokers have less risk of lung cancer than do plain cigarette smokers. Who smokes filter-tipped cigarettes? A different kind of person from the person who smokes plain cigarettes. Maybe they're a different social class. So Ernst has probably balanced that for social class. Maybe they're different age groups? He's probably balanced that for age groups. But perhaps they're people who inhale less, took in less tar and nicotine anyway, and therefore were the first ones to change.

WYNDER: Certainly, the filter cigarette smokers who are reported in literature do not inhale less than those who smoke nonfilter cigarettes. In fact, evidence that we have been accumulating in metabolic studies of nicotine in the bloodstream shows that, if anything, the filter smokers inhale more. But also, it is not just a small sample in terms of selection, it is a large sample in our study.

RUSSELL: The size of the sample doesn't seem to matter. It's the randomization and the selection that matters. I don't care whether the sample is 50,000 or 5000, it's how they've been selected.

WYNDER: But if we talk about selection, you have to show me the mechanism by which this selection would have etiologic significance. If you propose an alternate suggestion, it has to have a basis that is reasonable.

RUSSELL: Obviously it would have been ideal to take a large population and randomly assign them to one or the other for 10 years, but you couldn't do that.

WYNDER: Of course you couldn't.

RUSSELL: But perhaps that's what you need to do to answer the question. Just because that hasn't been done and can't be done easily, doesn't mean to say that you can answer the question by using nonrandom samples.

McELHENY: Aren't you, in fact, asking what proportion of the effect you can attribute to a decline in the incidence of smoking in a particular age group and how much is attributable to change in the composition of the cigarette?

BOCK: It's quite clear that you cannot get a mathematically precise answer for this question. All you're going to be able to get is the probability expressed by somebody who is intelligent and informed with respect to this point. And

I think . . . obvious that Ernst would say that probably a large number of the decreased cases is due to changes in cigarettes.

RUSSELL: Let's admit a wee bit of uncertainty.

KEITH: Well, in the last talk we heard today (Auerbach et al., this volume) there was some clear pathological indication that smoking the lower-tar cigarettes had improved the situation.

RUSSELL: Are we going on to question 3 now?

HOFFMANN: When Dr. Wynder said, "changes of the cigarettes," he did not commit himself to filtered or nonfiltered cigarettes. Changes in cigarettes during the last 20 years have been reflected in histopathological changes, but he did not commit himself to filtered or nonfiltered.

BOCK: Actually, you'd want to modify the evidence and say that some decrease in lung cancer is due to the fact that there are fewer lifelong smokers than there were 20 years ago.

SHIFFMAN: With regard to Dr. Auerbach's data for a moment, I don't think he said even that. He said that during the period in which cigarette composition was changing, an accompanying change in lung tissue pathology was observed.

SCHWARTZ: I think that one has to be very careful in interpreting the Auerbach data. First, there were two periods of time. We did not have any assurance that there was an absolute match of sampling sites between the two time periods. Second, if I were given slides that were prepared 15 years ago, I could identify them as 15-year-old slides; this would not be a blind study. Third, we have no case frequency data. Finally, there was no evidence construed or otherwise that the lesions shown are necessarily premalignant. So there are many reasons why one should be very conservative in interpreting this data.

McELHENY: Those points were raised at the time of the original study (Auerbach et al. 1961).

SCHWARTZ: Yes. I think they should be raised again, and they should be continually raised until such time as they are verified.

RUSSELL: Would you like to leave a question mark against question 2?

SCHWARTZ: Yes, indeed I would.

KEITH: If you go back to Larry Garfinkel's presentation this morning where he was looking at levels of tar and nicotine over two periods of time (Garfinkel, this volume), he was finding risk factor changes 60–80% of what they were 10 years ago.

HOFFMANN: And Dr. Schwartz spoke of the same histopathological repertoire

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20 years ago as now. The same man—Dr. Auerbach—read the slides both times, and both times he read them blind. So I don't know why Dr. Auerbach should have changed his method of reading histopathology in the past 20 years.

SCHWARTZ: Perhaps you didn't get the implication of this comment. Specifically, I believe I could tell which were the 15-year-old slides and which were the newly prepared slides. The colors of the fixative, the stains, the media, and the glass itself would all be different over a 15-year span. So it would be impossible for me to read those blind.

WYNDER: Well, with all due respect, Dr. Auerbach is a meticulous reader. That is probably not the problem.

But, I don't think the Auerbach study is related to question 2. One of the things that has always appealed to me about science is that if I find something that makes biological sense, then I feel reassured. Thirty years ago, when we had a 40-mg tar cigarette, if you smoked 30 cigarettes a day you were exposed to about 1200 mg tar a day. Today's cigarettes have 20 mg tar, so you are exposed to 600 mg tar daily. If there's one thing everybody can agree on, it is that all tobacco-related cancers are dose-related. If we cut the dose in half, wouldn't we be amazed if we didn't see some response in the reduction of risk (unless we compensated by smoking twice as much).

RUSSELL: But have you actually shown that smokers today have less risk of lung cancer than smokers of 20 years ago?

KUNZE: How could you?

RUSSELL: I'm not the epidemiologist. This isn't the kind of work I do. I want to know if cigarettes today are less carcinogenic than cigarettes of 20 years ago in the U.S.

GORI: When you speak of carcinogenicity, you're thinking of the specific activity of the tar and the dose of the tar. As far as dose is concerned, you probably can say that it is lower today.

ASTRUP: I think that the answer to question 2 is unclear. I would like to advise the epidemiologists and the chemists to study the conditions in Finland. The Finnish male population smoked the same amount of cigarettes in 1920–25, as the other Scandinavian males are smoking today. This difference in smoking habits is explained by the fact that the Finns learned to smoke from the Russians during the Crimean War; the other Scandinavians learned to smoke from the Americans and the British after the World War II. So there might be some interesting data to get out of the Finnish material.

WYNDER: If you smoke differently, for instance, like the Japanese who did not inhale, the risk of lung cancer will be reduced. But question 2 asks if there is evidence that these reductions in rate are due to differences in cigarettes. As I

indicated earlier, we have compared filter cigarette smokers (those lifelong smokers who switched in the past 10 years from nonfilter to filter cigarettes) with lifelong nonfilter cigarette smokers. And we demonstrated a reduction in risk of lung cancer of some 33% among the filter cigarette smokers, a finding confirmed by the American Cancer Society.

RUSSELL: But you've got self-selected samples. That's what we object to. Let's face it, it's a different person. Supposing you did that at a time when 50% of the population smoked filter-tipped cigarettes and 50% smoked plain cigarettes. If we can't say "yes" to question 2, let's admit it and go on.

BOCK: But the evidence is more than just that. You've limited this only to an epidemiological discussion. But, by itself, epidemiology must also take into account that what we know about carcinogenesis is from the study of other systems.

GORI: Also you may have to present evidence that addresses the question of, if not cigarettes, then what else?

RUSSELL: Quitting cigarettes.

GORI: Yes, but suppose there are other factors in the environment.

RUSSELL: Okay. Later we'll look at the discrepancies between laboratory evidence and epidemiological evidence.

HARRIS: I should add one thing in terms of temporal profile. The major change in the average tar of cigarettes occurred from about 1950 to 1965, as you will see if you just look at the plot of the sales-weighted average tar as it appears in the 1979 Surgeon General's Report (Public Health Service 1979). By 1965, approximately 60% of the smoking population were already smoking filter-tipped cigarettes, so that by 1975 most of those who continued to smoke had already smoked filter-tipped cigarettes for more than 10 years. However, the period from 1965 to the present is also the period in which individuals quit smoking entirely. So I expect that those facts should be important if you're trying to determine what would happen in the future.

RUSSELL: We don't want to dwell too long on one question. I personally am a little sobered by the fact that it has taken us so long to say "yes" to the second question and that we haven't been able to do so unequivocally. We've spent a lot of time straying to the third question, assuming the second to be true.

GORI: There is one other piece of evidence here. The consumption per smoker, in this country at least, has been going up slightly in the last 10 years or so, and nicotine yield per cigarette has been going down. This tends to indicate that among smokers the consumption and number of cigarettes consumed has remained constant or only slightly up and tar and nicotine have obviously gone down. So the average intake must have gone down at least in the

very heavy smoker who has reached a ceiling and cannot compensate.

RUSSELL: That is if you base it on number of cigarettes smoked and their machine-smoked yields.

GORI: Right. Well, what other data do you have?

KEITH: Actual dose.

GORI: Data on actual dose are virtually nonexistent.

RUSSELL: May we go on to question 3? If, in fact, cigarettes are now a little less hazardous with regards to their carcinogenic effect (we're not quite getting onto the coronary risk) is this due to the change in the quantity of tar they produce or the quality of the tar they produce? Are we actually able to answer that or not? If this is not an either-or question, are we able to weight it at all?

McELHENY: Can I ask a question? Didn't the work at NCI (Gori 1976) indicate that there was not really a change in the specific activity?

GORI: We really didn't test commercial brands. Our brands were experimental brands, so we can't make that kind of a conclusion.

McELHENY: It must be very difficult to change the specific activity.

GORI: You can change it 20–30%, no more than that. It's still insubstantial when you speak of dose-response.

McELHENY: What are you changing?

GORI: The activity of the tar.

HOFFMANN: I think what is more impressive is that over many years the same female Swiss mouse strain responded to 0.005% benzo[a]pyrene (B[a]P) with a constant rate of tumor-bearing animals in the groups. Year after year we painted mice with tars from the leading brands, and year after year we found a decline of tumorigenic activities on the basis of gram-to-gram condensate applied; that is a reduction of specific activity.

Now, you could have had changes in the strain of the random-bred Swiss mice, but then their response to B[a]P should also have changed. It didn't. Positive and negative controls have not shown any changes, but we have a change in the specific tumorigenicity. The numbers of mice in these experiments were in the hundreds.

SCHWARTZ: Is it not possible that they could have changed to the quantity as well as the quality of the tar?

HOFFMANN: No. I don't think there is any evidence that the strain would differentiate between the two, because the two went on simultaneously. As to the cigarette, the introduction of the cigarette filter changes the composition of tars.

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RUSSELL: If we say that changes in both quantity and quality of tobacco smoke are important, are we able to say which takes most of the credit?

BOCK: You can't get any decision on that from human data because the change has occurred simultaneously. There's no way you could tell from human observation.

SCHWARTZ: Can I ask a question? Of the countless components of cigarettes and smoke, how does one decide that these are the only components of relevance?

RUSSELL: The gas phase has many hundreds of components, the particles have thousands. We have talked a lot about quantitative changes in yields as measured by standardized machine smoking. To get it in perspective, I would like to compare the laboratory data with epidemiological data for: a large cigar; an untipped, plain cigarette; and a low-tar, low-nicotine, filtered cigarette.

Dietrich [Hoffmann], you're an expert. You've measured things in the smoking machine. Could you tell me the deliveries of a big Havana cigar. Roughly, how much tar would it push out?

HOFFMANN: The highest we ever got was 70 mg.

RUSSELL: All right, 70 mg tar. What are the nicotine and carbon monoxide (CO) yields?

GORI: You have to keep in mind the cigar itself acts as a filter.

RUSSELL: Okay. Shall we say the plain cigarette produces 25 mg tar and 1.8 mg nicotine? What about the low-tar filter cigarette?

GORI: It produces 10 mg tar, 0.8 mg nicotine, and 10 mg CO.

RUSSELL: Now, Ernst, you're the epidemiologist. What are the risks of smoking these three things?

WYNDER: For what disease?

RUSSELL: Lung cancer.

WYNDER: It's very important to stress that for cancer of the oral cavities the risk of cigars and cigarettes are about the same, indicating that cigars have plenty of carcinogenic activity. It's a question of inhalation. For lung cancer, as I said, we have no human experience to show what would happen if you would smoke the low-tar cigarettes for your lifetime.

RUSSELL: Then what if we were to change it to filter-tipped cigarettes, which are still lower than the plain?

WYNDER: But you know from dose-response data for 10, 20, 30, 40 cigarettes, years ago, that if you cut the dose in half you were likely to cut your risk in half.

HOFFMANN: This is being really technical. Nobody smokes ten Cuban cigars a day. But you can smoke 40 cigarettes a day.

RUSSELL: I'm just trying, perhaps rather crudely, to get across the point that what the machine says is not necessarily what the epidemiologist finds, because it's what the smoker does with the smoke that we have tended to overlook.

HOFFMANN: We can agree on that.

WYNDER: In other words, the cigar smoker—and this is really clear—has a relatively low risk of lung cancer unless he inhales. He also has a relatively low risk of coronary disease; and the plain smoker has a risk that goes up to one in ten if he smokes 40 of those cigarettes a day. What our study shows is that if you smoke a filtered cigarette for at least 10 years, your risk is reduced by one-third.

WATSON: What's the evidence that nicotine has anything to do with lung cancer?

WYNDER: Well, that came up earlier today (Bock, this volume). There is some question about this. I personally think it is not closely related to nicotine, though nicotine may affect your depth of inhalation.

RUSSELL: Exactly. So I think that quite clearly the strategy for a safer or less hazardous cigarette seems to be to identify the toxic products, the etiological agents for the various diseases that we know are caused by smoking, to work at that, and then to eliminate or reduce them as far as is possible without impairing the cigarette's capacity to satisfy.

So that we have two problems. First there are toxic agents that contribute little to satisfaction. This is an easy problem and is within the province of the cigarette engineers. We will get to that tomorrow. But it's where a toxic or harmful component contributes to satisfaction that we have a more difficult problem. We can't just look at what the smoking machine says. We need to find out how the person responds to reductions and how they affect acceptability and inhalation. For these reasons I was very interested in the talk we had this afternoon about the nitrogen oxides (Diamond, this volume), to see the huge variation in yield, and to hear that filters can selectively affect them. As far as I know, they don't contribute to satisfaction. So that's probably an example of an agent that could be reduced fairly easily.

But the big questions are how far can we reduce tar and how far can we reduce nicotine, and whether we can alter the ratio of tar and nicotine to lower the risks and hazards of cigarettes while maintaining acceptability and avoiding compensatory increases in inhalation. Before going on to these questions, perhaps we could move to CO. We had two speakers today on the subject of CO (Astrup; Schwartz et al.; both this volume). As far as I know, CO can be reduced and does not contribute to the satisfaction of the cigarette.

KEITH: The only practical means we have for reducing CO at the present time is

ventila...n, and this also affects all the factors that you would call satisfaction. So, it's a little more difficult to separate them.

RUSSELL: Presumably if we decided to reduce CO, rather than tar and nicotine, we could focus on diluting by ventilated filter.

KEITH: Those gains can be made and are being made.

RUSSELL: Yes. So it could certainly be done to reduce CO substantially while maintaining reasonable tar and nicotine, if we decided that that was useful.

GORI: But if you ventilate you reduce tar and nicotine, too.

GUERIN: You have to be careful. You have to take both. This discussion may be a bit academic. There are products on the market now that deliver only a milligram or two of tar, a few milligrams of CO_2, and tenths of a milligram of nicotine. It not only can be done but it is being done, and the products are selling to some degree.

RUSSELL: The point is that maybe they're not smoked because they're low in everything, and we're saying that it might not be possible to lower the things that contribute to satisfaction. If we find we can't lower tar and nicotine without loss of acceptability, perhaps we could still lower CO yields if we thought this would be a health advantage.

BOCK: That's clearly a prospect. In 1955, the cigarette industry people I talked to were unanimous in saying that you could never market a cigarette delivering 15 mg tar. It's obvious that they can sell just about anything when they do it gradually.

GORI: Two years ago the cigarette industry was telling me adamantly that they could not produce a cigarette with a tar-to-nicotine ratio of less than 10:1, and to date there are some on the market that go far beyond that. I believe that practically everything is possible, if we give the market time to adjust to the changes that are going to be introduced.

McELHENY: We are likely to hear tomorrow that in a year's time the market share of cigarettes under 15 mg moved from less than 30% to more than 40% of the American market (Maxwell, this volume).

RUSSELL: I would like to move to CO because of its disputed role in cardiovascular disease, vis-à-vis nicotine, and whether or not (I was assuming not) it contributes to satisfaction. If it were found to be an important cause of coronary heart disease (CHD), peripheral vascular disease, and cerebral vascular disease; it would be easy to reduce it providing it makes no important contribution to satisfaction. Gio has expressed some doubts as to whether it would be easy to reduce CO.

GORI: No, no. I think that it can be reduced.

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RUSSELL: I don't mean that it cannot be reduced in a cigarette, but can it be reduced without loss of acceptability and compensatory increases in inhalation, etc.

GORI: I would think that perhaps 5% may be that threshold below which there is no measurable effect, carcinogenic or otherwise, except perhaps in certain individuals.

RUSSELL: You're pontificating now.

GORI: I'm putting it up for discussion.

RUSSELL: I know of no positive evidence that it's psychologically rewarding to have your COHb fluctuating at about 8.5%.

GORI: Let's think about the toxic and carcinogenic effects of COHb below 5%.

RUSSELL: All right. I was very interested in the two talks we heard. Dr. Astrup (this volume) doubts that CO was an agent in the harmful effects of smoking during pregnancy. He also discussed whether or not it was harmful or contributed to arteriosclerosis. As I have read the evidence, I don't think that anyone at present can say how much CHD and arteriosclerosis are due to nicotine and how much are due to CO. I think we're in a sad state, and I was quite encouraged by Dr. Schwartz's work (this volume), although it didn't seem that his monkeys were inhaling because they never had high COHb levels. But if he does get his baboon model going it will be a very good model. If he can produce any pathology in his smoking baboons that is at all comparable to vascular disease in humans, his model will be ideal for administering CO separately from intravenous nicotine to distinguish which of the two causes pathological changes that may have a relation to the condition in humans.

I wonder if I'm right in assuming that it's uncertain as yet whether nicotine or CO is implicated in cardiovascular diseases?

GORI: I think you can say it's uncertain whether CO is implicated in cardiovascular disease. As far as I'm concerned, we can forget about nicotine for a moment.

BATTISTA: It depends on whose paper you're reading. If you're looking at the effects of CO on subjects who have already had coronaries, then the CO is thought to reduce the amount of oxygen available to the coronary circulation. This makes one predisposed to myocardial infarction, heart attack, or what have you.

RUSSELL: I think that's fair enough. There is evidence that it causes some exacerbations of established CHD.

HOFFMANN: This is in an acute mode. But can we speak of a pathogenic effect in a chronic mode? The evidence is practically nonexistent.

RUSSELL: Would you agree with that, Dr. Astrup, that we can't say how much it's CO and how much it's nicotine?

ASTRUP: I think it has an effect on the myocardium.

BATTISTA: I tend to believe that normal levels of CO are not that important in the healthy or normal smoker.

SCHWARTZ: I think the data base is inadequate, Mr. Chairman.

RUSSELL: It would seem to be very important to do research of the kind that you're doing, since CHD disease is a major "smoking killer," and we're not sure which of the two agents is mostly responsible.

McELHENY: Isn't it fair at this point to ask, for completeness, whether there is any epidemiological evidence that points to a reduced cardiovascular risk from anything that's happened to the cigarette, or changed patterns of smoking, or the changed incidence of smoking?

HOFFMANN: That was presented by Dr. Hammond (Hammond, this volume), who showed a 20% reduction in coronary death with filter cigarette smoking. I pointed out at least two other factors that must be considered, namely serum cholesterol and blood pressure treatments, which may be better in the person who smokes filter cigarettes because he's more educated.

I think the crux of this is to what extent can or should we reduce nicotine? Metabolic epidemiological studies indicate that the catecholamines released subsequent to smoking relate principally to the nicotine content of the cigarette (Armitage 1965). Sudden death, which is principally due to ventricular arrhythmia (Schwartz, this volume), could be related to a nicotine-induced catecholamine arrhythmia. I would suggest that this is probably the way it works. It is for this reason that I would not be in favor of a low-tar, high-nicotine cigarette. We are currently involved in studies to determine whether more catecholamines are released when there is more free nicotine in the cigarette.

RUSSELL: We don't know that release of catecholamine is harmful. Every time you have sexual intercourse catecholamines go up, every time you give a lecture they go up, and every time you jog they go up. Are you going to say that all this causes CHD?

WYNDER: This is true, Mike [Russell], but we both know that you get catecholamine release eight times per cigarette. If you smoke 20 cigarettes, that's 160 times a day. This is really what makes cigarette smoking so unique: the pulsating dose of nicotine and catecholamine you get throughout the day, and you get this within seconds after you smoke.

McELHENY: What's the minimum amount of nicotine that would give you some semblance of that?

WYNDER: The preliminary results of a study recently completed by Dr. Hill

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(pers. comm.) in our laboratory showed it was 0.6 mg nicotine per cigarette. Since we now have better techniques for such a study, we are in the process of repeating the study.

SCHWARTZ: Has anybody undertaken studies in which they have experimentally produced minor degrees of myocardial ischemia, and then exposed the animals to small relevant doses of nicotine.

GORI: In spite of all our talk of sudden death and cigarette smoking, there are a number of people at the Heart and Lung Institute who are skeptical about this sudden-death syndrome, because nobody has yet found anyone who has been a victim of sudden death with a cigarette in his hands.

WYNDER: First of all, sudden death is an important public health problem because 40% of all myocardial infarction is sudden death. Secondly, the Framingham study shows that the greatest risk among smokers was for sudden death, much more than for fatal heart attacks, and even greater than for those who survive the heart attacks (Kannel et al. 1968).

RUSSELL: Gori is saying sudden death is not coming at the surge of the blood nicotine and catecholamines in smokers. It doesn't come at the time they're getting that surge.

GORI: It doesn't occur in an acute mode.

WYNDER: The person who smokes 40 cigarettes a day is a heavy smoker. He's putting out a lot of catecholamines throughout the day.

DIAMOND: Recently, we've performed some experiments at our laboratory that you can relate to this. We have taken the coronary artery from horses, suspended the arteries in a tissue bath, and monitored their contractile activity. We also obtained dose-response curves for the catecholamines. Then we incubated these same tissues in various concentrations of nicotine, and repeated the same dose-response curves to catecholamines.

The objective here is to find out whether or not the presence of nicotine would alter the sensitivity of the coronary arteries to endogenous catecholamines. We were unable to detect any difference in the dose-response behavior of these tissues to norepinephrine or to epinephrine in the presence of nicotine. In addition, we found that nicotine alone does not affect the contractile state of coronary arteries nor does it alter the calcium kinetics of the exchange of calcium between extracellular and intracellular fluids. So that I think we have to look elsewhere besides nicotine, at least for changes in contractile activity.

SCHWARTZ: One point of potential relevance relates to the role of plated microemboli and the possible influence of the nicotine-catecholamine axis. There's little doubt that −10 M concentrations of catecholamines are able to potentiate adenosine diphosphate (ADP)-induced platelet aggregation in vitro, where the concentration of ADP alone is unable to induce aggrega-

tio. ..der certain circumstances, very minute quantities of catecholamines may be released as a result of nicotine release, or stress. This could result in intravascular platelet aggregation, the resulting platelet microthrombi or plated microemboli causing transitory obstruction and microfocal ischemia. This could well set the stage for the development of lethal arrhythmia. Such microemboli are found within the significant proportion of patients dying suddenly and unexpectedly lending support to the potential importance of such mechanisms.

WYNDER: Let me just point out a very important epidemiological observation—an observation first made by Ancel Keys (1970) in Yugoslavia. The observation is that a population with a low serum cholesterol level has no increase in CHD due to heavy smoking. So the heavy tobacco use only affects an individual already with coronary artery disease due to hypercholesterolemia.

SCHWARTZ: The same is true of hypertension. There is an independent hypertension effect in the presence of an elevated plasma cholesterol level.

RUSSELL: I feel that we've left the animal experimenters out of this discussion a bit. Their work has identified many of the agents in tar that are carcinogenic. I think we agree that we'd like to reduce tar as much as possible in quantity, with an eye on what that does to acceptability. The feeling is that flavor additives might help to overcome the acceptability problem.

Another point is that we admit the quality of tar has changed for the better. Has this been just by chance processing, or has it been part of a deliberate strategy to work at (by processing filtration etc.) reducing the agents that we think are carcinogenic? I realize that extrapolation from various animal models to humans has its problems. Should we be doing more to try deliberately to change the quality of the tar as well as the quantity of it? Has anyone got any comments?

GORI: Well, there is an economic incentive to decrease the amount of tobacco that goes into a cigarette, and you can see that progressively over the past years the poundage of tobacco that goes into cigarettes, at least in this country, has decreased considerably. The manufacturer can now make many more cigarettes with a pound of tobacco than he did before. In a sense, this decreases the amount of fuel per cigarette and therefore the emission of smoke.

RUSSELL: You make it sound as if that's come about by chance.

GORI: No. There is an economic incentive but it is not the only one; there are others that have been pointed out by a variety of studies. At the National Cancer Institute, we tested various manipulations of the tobacco (Gori 1976). Dr. Tso has studied several varieties of tobacco in the fields and different curing methods. All of this has pointed out some feasible ways

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of manipulating the tobacco so that we may come up with less smoke, less fuel, less smoke emission, less specific activity, and a better utilization of the tobacco.

RUSSELL: Are we doing enough? We're publishing figures on the different amounts of tar that cigarettes produce. Should we be looking at the different agents in tar, the qualitative differences between brands on the market? Should these be published, perhaps?

GUERIN: It's just impractical. A few additional constituents might be measured and reported. I believe we need, however, a practical means of surveying the tar and perhaps the gas phase of smokes to determine whether unusual constituents are present and to ensure ourselves that manufacturing practices adopted to provide ultralow-tar and nicotine deliveries have not also changed the overall chemical nature of the resulting smoke. We must be certain that today's tar is essentially the same material as yesterday's tar if we hope to use today's epidemiology to judge success and set directions.

RUSSELL: A lot of it would be known from the constituent tobaccos would it not?

BOCK: Aside from nicotine, there is no constituent in tar that is shown to be related to its biological activity, in terms of producing cancer.

RUSSELL: It's not a very easy task then. We've got to leave it to chance, have we?

WYNDER: No, I do not believe that. Dr. Hoffmann (Hoffmann, this volume) estimated what we feel should be maximal levels of harmful smoke constituents. We have chosen certain individual compounds as indicators of classes of substances with potential biological activity. B[a]P is the indicator for tumor initiators of the polycyclic hydrocarbon type, phenol and catechol are indicators for weakly acidic tumor promoters and cocarcinogens respectively, hydrogen cyanide (HCN) is the most toxic gas-phase constituent, etc.

I would not be in favor of listing all harmful smoke constituents on the cigarette pack because nobody would take notice anyway. But I do believe that we should give industry some guidelines as to maximum levels for about six or seven indicators. I think that everyone here could agree upon this.

BOCK: In the 50 or so samples they gave me, the B[a]P content was inversely proportional to the biological activity negative ion. Now, what are you going to do—

WATSON: What's the biological model?

BOCK: Mouse skin carcinogenesis.

RUSSELL: Okay. So it's difficult to work specifically on the quality of the tar then, other than the fortunate fact that processing and puffing it out to

impro... filling power for economic reasons seems to have had some health advantages too.

HOFFMANN: That's not true. I am really irritated because we, as scientists, don't know about economic factors. That's not our business. Our business is not to sell cigarettes, but to make cigarettes less toxic. I must say I'm slightly upset, after playing around with this for 20 years, to listen to the story that things are economically unfeasible.

As Dr. Wynder stated, when we started, filtered brands comprised 5% of the cigarettes on the market. Today they are 90% of the market. The perforated filter significantly reduces CO. Five years ago, it was zero percent of the market. Today it comprises 20% of the U.S. market. I do think the tobacco industry, voluntarily or not, adjusts very well to the demands of the logical reasoning of the scientific community and that we should continue on this path.

When it comes to tar there are two factors to consider. One is how to make the combustion more complete. The other factor relates to certain components in the tar that do not evolve from combustion but are leaf constituents that transfer into smoke by distillation and vaporization. Depending on leaf composition, there are many opportunities to modify tar composition, beginning with tobacco selection.

I like to emphasize that reduction of tar includes modification of the combustion, as well as modifying the composition of tobaccos in respect to semivolatile and distillable leaf components. But we have ways and means to accomplish this.

I don't think that we should get confused with a lot of economical factors. Low-tar, low-CO, low-nicotine cigarettes obviously sell, because they are close to 20% of the market. If we continue on our path, they will eventually constitute 90% of sales just as the filtered cigarettes have done within the last 25 years.

RUSSELL: You're happy then with the way things are going, with merely reducing everything as much as possible?

HOFFMANN: I'm even happier now having heard today that the low-tar, low-nicotine cigarette smoker is more likely to become an ex-smoker than the high-tar cigarette smoker. So we have two ways. I think our job is to spend research money to reduce harmful smoke constituents, and not to worry about economy or marketing problems of cigarettes.

RUSSELL: Okay. So Dietrich feels that one can reduce pretty well everything.

GORI: We have an entire session on that tomorrow, and you can make cigarettes that effectively emit hot air today.

RUSSELL: That's right.

HOFFMANN: Beautiful. We have reached our goal.

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GUERIN: I believe that the industry has paid much attention, as a matter of fact, to purposely not manipulate tar composition dramatically. It relies on knowing something about the biological activity and consumer acceptability of this tar. Substantial changes in composition could be accompanied by greater biological activity per unit mass of tar and would jeopardize the utility of the existing data base to guide further developments.

McELHENY: So they would have an incentive not to vary it.

GUERIN: I believe they've done remarkably well in maintaining the general composition of tar and, at the same time, reducing its delivery per cigarette quite dramatically.

SCHWARTZ: May I just ask a question? We have just heard a statement that there was no clear relationship between this biological testing and the nature of certain components of tars in the specimens submitted. This raises a very important question and has at least two important implications. First, the biological testing programs may themselves be inappropriate in assessing the toxicity of the tars. Secondly, we're not studying the right tars, or their components. I think that we should really address this question very seriously.

BOCK: Well, it's difficult to say that a carcinogenic test is inadequate to measure carcinogenicity. We're talking about mouse skin, you know, and there maybe some other test.

WATSON: You're saying, though, that B[a]P....

BOCK: I'm saying that in the only large-scale study of this sort, which was run by Dr. Gori (1976), aside from nicotine, no constituent of cigarette tar was correlated with the long-term carcinogenic activity.

WATSON: How did the mouse-skin test correspond to the in vitro tests?

BOCK: They don't compare, because they're testing two different things. The Ames *Salmonella*/microsome assay is trying to test mutagenic materials, and the process of carcinogenesis involves much more than that in the case of cigarette tar, where the mutagens are probably minor components.

WATSON: Why do you believe that?

BOCK: Because when we look at the material, it behaves more like a tumor promoter or like a cocarcinogen.

RUSSELL: Does anyone think that any of these constituents of tar contribute in any significant way to satisfaction?

CAIN: It's the aldehyde content.

RUSSELL: So to reduce these constituents would reduce satisfaction?

BATTISTA: It would change it anyway.

GORI: It would change the irritation from the smoke, which is part of the satisfaction.

CAIN: The major appeal of the cigarette as a sensory stimulus is on the common chemical sense, not on taste (Cain, this volume). The major element of satisfaction is a feeling factor or some aesthetic event, and insofar as HCN or nitrogen oxides contribute to that, then it is presumably contributing to that level of enjoyment that the smoker sets up initially as a kind of criterion event.

BOCK: I'd like to go back just one step to ask whether all reductions in cigarette risk are designed. One of the things that present technology seems to show as an improvement is reconstituted tobacco sheet (RTS). This advance was fortuitously employed because it reduced the costs of manufacturing the cigarette. The method was used to recover lost material. Can this process be extended? Is RTS now being made deliberately using whole tobacco leaf?

TSO: Not only does RTS use the waste material, but it also changes the physical property of the burning material. You can reduce the combustion product, and as you were saying, reduce the tar.

RUSSELL: We have to end now. I don't think we have come anywhere near answering our questions. We haven't finished our meeting, but I hope that tonight we've tried to focus on some of the questions that must be answered if we're going to come up with a prescription for a less hazardous cigarette. If we are to make substantial further progress towards this goal we must consider the factors of acceptability, satisfaction, and self-regulation as well as crude toxicity. We must not ignore any of these areas.

Thanks very much.

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A Summary Appraisal

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Evidence has been presented at this meeting that could justify further promotion of less hazardous cigarettes as a major public health endeavor.

The major alternative to less hazardous cigarette promotion has been the smoking and health education effort over the last 20 years. Success of this effort has been difficult to measure because a control scenario does not exist. The impact appears mild in the United States. In the last 20 years, consumption per United States resident has not decreased—stabilizing recently at about 4000 cigarettes per year—and consumption per smoker has continued to rise to some 12,000 cigarettes per year (Federal Trade Commission 1979).

In contrast, a most dramatic event in the history of cigarette smoking in this country has been the reduction of sales-weighted averages of tar and nicotine delivery per cigarette to about half the values of just 15 years ago.

Because of this reduction in tar and nicotine delivery, concerns about what is called compensation are moderated. Compensation, the smoking of more cigarettes or deeper inhalation of cigarette smoke by smokers switching to milder brands, has been demonstrated in experimental settings. But the change in tar and nicotine delivery has been so large that it is plausible that the average smoker of today inhales far less smoke and tar and nicotine than some years ago (Garfinkel 1979). The reduction is probably more significant for heavy smokers at high risk, who smoke all the cigarettes they can manage daily.

Hence, it is attractive to accept the conclusions of many epidemiological studies that users of low-tar, low-nicotine cigarettes—usually filtered—show a reduced risk of disease roughly proportional to their reduced smoke intake. Studies presented at this meeting by Hammond, Garfinkel, and Wynder illustrated this with dramatic evidence ranging from morbidity and mortality surveys to direct observation of histologic slides.

The trend in the reduction of tar and nicotine does not show a slackening. It may likely accelerate during the next few years. Hence, it is reasonable to expect that future epidemiologic studies will continue to sustain the conclusions and inferences presented during this meeting, and show an increasing

decline o[illegible]king-related diseases. This prediction is reinforced by the early studies in England showing an actual reduction of lung cancer rates, and by incipient signs of improvement in this country, starting with impressive reductions in the incidence of cardiovascular diseases, respiratory illnesses, and with a noticeable change in the still positive lung cancer rates at young age groups, at least for males.

Smoking is perhaps the best studied modern risk factor; one for which the most extensive epidemiologic evidence has been accumulated over the last three decades. This massive record, unique among risk factors today, makes it possible to forecast with unusual confidence real-life dose-response functions in humans, and to infer what the desirable goals might be in reducing the smoker's risk to minimal terms.

In the regulation of many risk factors it is accepted as axiomatic that tolerable levels of exposure (TLVs in toxicologic language) are those at which the risk is not distinguishable from that of the nonexposed (Lynch). Epidemiologic evidence of unprecedented magnitude and consistency seems to indicate that such TLVs exist for smoking as well (Gori 1976). It is clear that these levels must have different significance for the average smoker and for special groups at high risk, nevertheless they should remain realistic goals of public health policy (for further discussion, see Kunze). Today, cigarettes that would make it possible to obtain such goals are available on the market, but few of them have obtained the widespread acceptance that could warrant hope for a reduction of risk below detectability. Before that goal may be reached, a vast amount of research and patient persuasion of public awareness appear necessary.

Research could proceed in three main directions. First, it will be necessary to continue the toxicologic characterization of smoke and smoke components to provide a more detailed background for epidemiologic studies. This would also promote better efforts in a second direction: the design and engineering of desirable changes in the cigarette to bring about the reduction of selective smoke components, the specific activity of the smoke, and total smoke delivery. A third direction would be to explore those behavioral characteristics of the smoker that determine his interaction with a cigarette and, by extension, those phenomena of compensation or titration that may occur when a smoker switches to a cigarette which has diminished flavor and pharmacologic impact and so may partially neutralize the beneficial effects expected.

Some excellent reviews of past and present studies in the fractionation of carcinogenic and other components and their identification—from polycyclic hydrocarbons to volatile and nonvolatile nitrosamines, polonium-210 and lead-210—and the various interactions of cocarcinogens, promoters, and inhibitors of carcinogenesis were presented (Van Duuren, Hoffmann, Harley, and Bock). It was shown that the etiology of cardiovascular diseases is determined by several risk factors, a situation that makes it difficult to ascertain the smoke's share of responsibility (Schwartz). Previous theories that appeared quite solid, have been reversed by recent new findings. Dr. Astrup made quite clear the

reasonable doubt about the responsibility of carbon monoxide (CO) in the pathogenesis of cardiovascular diseases, except for possible acute toxic effects when the myocardium is already damaged by other insults.

Likewise, the role of nicotine in cardiovascular disease pathogenesis and in sudden death is still questionable. The demise of certain theories of pathogenesis, fashionable until recently, leaves a most distressing void in the understanding of the possible contributions of smoke components such as nicotine and CO, which by their acute toxic characteristics would be expected to exert major roles. This void is most uncomfortable and research in this area should be given high priority. The theory that atheromas could originate by mutational processes similar to carcinogenesis, and eventually result in the formation of atherosclerotic plaques, has intriguing aspects and should be tested in depth; it could provide a link between smoking and the increased risk of cardiovascular disease that epidemiologic studies have consistently uncovered (Battigelli).

Additional uncertainties plague our understanding of the pathogenic relationship of smoking and respiratory diseases. Research has been unable to pin a firm responsibility on the role of nitrogen oxides and other postulated mechanisms ranging from the effects of smoke on pulmonary macrophages, on mucociliary mechanisms, and on the levels of alpha antitrypsin, to the possible promotion of fibrinogenic and thrombogenic phenomena and the triggering of local immune reactions (Diamond).

The [redacted] strengthening. [redacted] which may act on the cardiovascular and respiratory system is embarrassingly [redacted] contradictory. The situation is particularly serious in the case of nicotine because although a reduction across the board for most smoke components, regardless of specific selectivity, has been a justifiable approach, nicotine appears to have a unique role in the pharmacology of cigarette acceptance. A better knowledge of its chronic toxicity is needed in the definition of less hazardous cigarettes.

Uncertainty [redacted] components may be greater than ever today, perhaps with the exception of some factions that have shown carcinogenic activity in animals. [redacted] difficult to provide a rationale for [redacted] of [redacted] aside from the self-fulfilling claims that the reduction of one or the other component may lead to reduced risk. Additionally, [redacted] not surprising that the most practical method is to reduce total smoke [redacted] and therefore all smoke components, [redacted] that are considered harmless and would restore desirable characteristics of acceptability.

Extensive tests conducted during the last 10 years by the National Cancer Institute's Smoking and Health Program began to define some modifications of tobacco and cigarette engineering that may not affect single specific smoke

compo but may reduce certain classes of them, thus reducing the probability of toxicity with a degree of selectivity. Several papers presented at this meeting reviewed the most successful of these approaches ranging from genetic selection of the tobacco plant, its cultivation and agronomic practices, to curing, aging, and various tobacco transformations (Tso).

Tobacco can be manipulated to reduce certain fractions which, upon combustion, may produce undesirable smoke components. The extractions of proteins, lipid and alcohol soluble materials, of nitrates, etc., belong to this class of efforts (Eicher and Müller). Most of these approaches are made easier by a process that involves homogenization of the tobacco and its reconstitution into suitable paper form after extraction or treatment (Selke). In general, these transformations cause severe deterioration of acceptability, and it is likely that they can be only partially utilized in the manufacture of cigarettes, at least until better methods for the safe reconstitution of flavor and acceptability may be defined. A successful approach to reducing the toxicity of smoke, in the particulate or the gas phase, involves the retention of smoke components by suitable filters, and engineering devices to reduce the amount of tobacco burned during puffs and dilute the mainstream smoke (Keith). Filtration technology has progressed significantly during the last 10 years but may have reached a plateau. The mechanical capacity of filters to retain smoke particles is generally excellent. The gas phase can be less affected since phenolic compounds and nitrosamines can be selectively removed by cellulose acetate filters. Activated charcoal inserts can provide selective retention of some other components.

Greater filtration efficiency is usually attended by undesirable pressure-drop characteristics at the mouthpiece, a situation that can be compensated by smoke dilution. In fact, cigarette ventilation and smoke dilution are among the most important devices currently in use for improving less hazardous characteristics of cigarettes (see Guerin and LaVoie). Ventilation is achieved either by perforations at the mouthpiece that relieve pressure drop by giving direct access to ambient air, or by high-porosity cigarette papers which essentially achieve the same result by permitting a faster entry of air throughout the cigarette rod. Both approaches achieve synergistic effects in the reduction of smoke and smoke toxicity.

Ventilation and dilution do not seem to affect nicotine as much as other smoke components, with the result that usually a gain in percent nicotine delivery is observed. Probably the principal effect of cigarette ventilation is the reduction of the amount of tobacco burned during puffs. Other ways to reduce the amount of fuel have been developed and include the puffing of tobacco and the inclusion of inert extenders, such as clays or carbonates, in reconstituted tobacco sheets. Both devices increase the filling capacity.

It is not surprising that all these cigarette manipulations should result in a deterioration of acceptability characteristics. Today it is possible to produce cigarettes that do not deliver any appreciable pharmacologic or organoleptic message. On the other hand it is clear that if less hazardous cigarettes are

expected to exert a major role in public health, they should be made to retain sufficient flavor to induce the smoker to accept levels of reduced risk. The intuitive proposition that the smoker should be asked to gradually reduce his intake by successive selection of cigarettes of increasingly lower toxicity is sustained by much published research and by the evidence presented at this meeting (Jaffe and Shiffman). Abrupt changes in consumption habits and standards of acceptance are either likely to cause compensatory phenomena, or to discourage the smoker from ever attempting more successful gradual approaches.

Fortunately the level of acceptability and satisfaction that a smoker derives from a cigarette does not seem to be strictly dose-dependent. For instance, today's average smoker is smoking cigarettes that would have not been considered adequate only 10 years ago, and, there is ample evidence that the average levels of acceptability can remain nearly constant if the dose is decreased in gradual imperceptible steps over a relatively long period of time. This seems to hold true for both major elements of cigarette acceptability—the organoleptic or flavor impact—and the pharmacologic action of nicotine. Clearly there would be lower limits, or thresholds, below which satisfaction and satiation would disappear, and research to establish these levels could be most useful. A cursory appraisal makes it appear that these levels are considerably below current sales-weighted averages of smoke delivery in commercial cigarettes. We still may have a long way to go towards further reduction of smoke emission before reaching levels below which the smoker could not be persuaded to accept milder products. Current and future efforts (as reported by Cain) in the preservation and restoration of organoleptic characteristics of cigarettes are likely to focus on the imaginative use of tobacco blends; in the subtle utilization of opportunities inherent in the ventilation of cigarettes; and, of course in the study, selection, and use of specific flavors and enhancers that may restore or amplify the taste and smell. It is generally reassuring that they are used in very minute quantities, in the order of one part per million in the tobacco blend, and therefore in even lesser concentrations in the smoke itself. Moreover their imaginative use could allow the reduction of other traditional additives to cigarette blends, which may have given reason for concern in past toxicologic studies (Gori 1980).

From various presentations at this meeting it is clear that many individual smoke components, which per se may have certain demonstrated biological activities in man or animals, behave quite differently in the context of smoke, because of multiple synergistic or antagonistic interactions. And so, it would be unrealistic to assess the biologic effect of any smoke component or additive as an independent entity, outside of the interactions that occur in smoke. The only reasonable approach would be to test extensively the entire smoke to which certain components have been added. The traditional assays of skin painting, ciliatoxicity, and other tests supplemented by extensive chemical analysis are likely to be of help, but the development of inhalation tests in larger animals

during the last years has made available methods that, although lengthy and costly, provide the only defensible evaluation of smoke toxicity (Bock and Battista). Parallel research during the last few years has also demonstrated that properly selected human subjects can be a most useful tool in the assessment of acute respiratory toxicity.

At the end of this review one cannot avoid a special consideration for nicotine which, besides being a major contributor to the taste and smell of smoke, is the most important pharmacologic principle in the complex relationship of the smoker and the cigarette (see Russell). A central question for nicotine regards its chronic toxicity, about which little is known in spite of a vast amount of research. Studies now in progress under the Smoking and Health Program of the National Cancer Institute aim at resolving this question. Should nicotine be found to have only minor chronic significance, as the case appears to be, then tar reduction and nicotine preservation would be desirable objectives for less hazardous cigarettes. This approach presumably would provide satiation to the smoker, reduce his propensity to either smoke more cigarettes or take deeper compensatory inhalations, and at the same time reduce other undesirable components.

Most commercial cigarettes in the U.S. have maintained a ratio of approximately 1:10 between nicotine and tar delivery in cigarette smoke, but in the last few years new generations of cigarettes have begun to apear on the market where the ratio of nicotine to tar has been pushed to as low as 1:5 or less. This approach seems plausible also because it appears that the chronic toxicity of nicotine may be far less than the chronic toxicity of tar, a consideration which by itself would justify altering the ratio of tar and nicotine in the smoke. Nicotine is not completely harmless. It will always maintain fearsome characteristics of acute toxicity, but a vast epidemiologic record suggests the presence of no-adverse-effects thresholds, even though these levels are considerably below the current average nicotine intake in smokers. Fortunately, the satiation levels for the pharmacologic action of nicotine may not be strictly dose-dependent and could be sustained if the dose is gradually decreased over a long period of time. Again, this conclusion is justified by the general acceptability of current cigarettes which are half as heavy in nicotine as those of just 10 years ago. Thus it may be possible to reach levels of nicotine concentration in the smoke that are still pharmacologically satisfactory, but so low as not to pose significant concern.

The progressive reduction of the nicotine-to-tar ratio in commercial cigarettes is a feasible but not a simple proposition. It may require changes in tobacco varieties and agricultural practices in the field of tobacco processing and blending, and fine tuning of filtration and ventilation practices, before the ratio could be favorably altered for the majority of cigarettes on the market as suggested by Tso.

What is the future of less hazardous cigarettes? Apparently we may look forward to further decreases in average values of smoke intake and to progres-

sively lower points of acceptability equilibria between tar and nicotine delivery, along with flavor characteristics that may still be perceived as satiating by the smoker. Maxwell's long observation of the market trends brings good news about changes in consumption patterns that are likely to accelerate, and the industry has been increasingly backing the advertising of low-tar and nicotine brands. Public policy in smoking and health has been dominated for years by idealistic approaches with moderate sympathy for less hazardous cigarettes.

One can hope that polarized attitudes may some day give way to a more realistic appraisal of the situation, particularly if the next few years will show a decline of smoke dependent diseases as a natural consequence of the declining intake of smoke, tar, and nicotine by the average smoker. The achievement of complete prevention goals in smoking and health would add a perceptible increment—2 years—to average longevity. That these gains should be costly is not surprising. In the socioeconomic and demographic framework of our society, living longer would aggravate current trends toward an aging population, further burden dependency ratios and pension plans, add to unemployment, and foment competing causes of mortality (see Richter and Harris). Yet, humanistic societies have always been ready to find new ways to fulfill the rightful aspirations of their members for healthier and longer lives.

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